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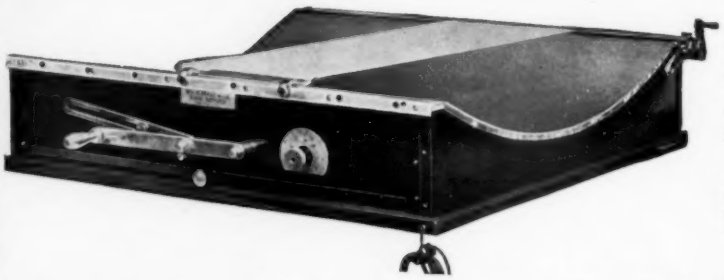

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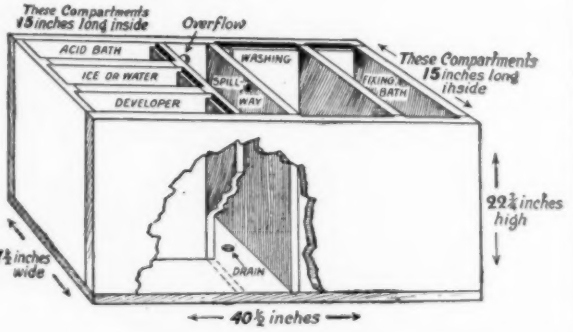

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THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

VOL. X OCTOBER, 1923 No. 10

RADIUM TREATMENT OF TOXIC GOITER WITH METABOLIC DEDUCTIONS*

BY R. E. LOUCKS, M.D., C.M.

DETROIT, MICHIGAN

IN order that the true significance of a pathological condition or dysfunction of the thyroid gland may be understood, it is absolutely necessary that the anatomic relation with physiologic function and normal metabolism should be known, with a comprehensive understanding of its relation to the other endocrine glands.

Anatomically the gland consists of two lobes connected across the second and third ring of the trachea by an isthmus. The posterior surface is in contact with the thyroid and cricoid cartilages, the inferior laryngeal nerve, the inferior constrictor of the pharynx and the lateral borders of the trachea and esophagus. The outer surface is covered with the superficial muscles of the neck and the external jugular vein. The outer border of each lateral lobe is in close proximity to the carotid sheath containing the common carotid artery, the internal jugular vein and the pneumogastric nerve. The significance of this relation is apparent when dealing with any one of the enlargements of the gland.

The physiological function appears to control the iodin and calcium balance and split up iodin products into thyroxin (Kendall) which acts as a hormone stabilizer to the whole endocrine chain. The one or the many hormones have specific function in cerebration of the brain cells, increasing the activity of nerve transmission and regulating the heat mechanism; in fact, they are the main activators of metabolism.

Normal metabolism signifies a harmony in all the functions of the living body that go to make up a "well being." A physiological activation is not by any means a pathological hyperactivity.

The question arises: When is a hyperactive thyroid a pathological disease? The answer: When symptoms of toxicity are manifest, either objectively, subjectively, or by laboratory calculations.

Suffice to note that a toxic goiter may be:

1. A primary exophthalmic,
2. A toxic adenoma,
3. A toxic adenoma with exophthalmos.

1. The objective symptoms are manifest in the exophthalmic type by (*a*) the prominence of the eyeballs, giving a staring expression and a facies of mental alertness, (*b*) a lagging of the upper lid in looking down so that it apparently covers more than its half of the eyeball when closed. At times the lids cannot cover the ball completely but leave a slit allowing the conjunctiva and cornea to become injected from exposure, lack of palpebral lachrymation and massage. A strip of white sclera shows between the cornea and lower lid when the eye is open. (*c*) There may also be winking, tardiness of external ocular muscles and decreased lacrymation. (*d*) At times a red tremulous tongue is found and also teeth notched on the lateral borders.

* Presidential Address read at the Annual Meeting of THE AMERICAN RADIUM SOCIETY, San Francisco, Calif., June 25–26, 1923.

The primary exophthalmic type may not show any noticeable change either in size or figure of the gland, while the adenomatous type presents variations in size, from the large prominent uneven mass to small lobulated cystic out-croppings on the lobes or isthmus.

Pulsations of the thyroid arteries are common and a bruit may at times be heard over either lobe. The radial pulse varies from 90 to 160 and often registers much less than the apex beat, as each wave does not have time to be carried independently.

The heart may be enlarged in all diameters and if the case is of long standing there is evidence of myocardial degeneration, as elicited by the degree of fibrillation and the character of the murmurs present. The precordial impact may be diffuse, and have enough force to cause a heaving of the chest wall with each contraction of the heart. Pulsation of the superficial arteries of the fingers and toes is common.

The systolic blood-pressure in primary exophthalmic cases is at first raised, but gradually returns to normal or goes below normal after the first crisis. Should a spontaneous cure succeed, it remains low; but should a second crisis occur it again rises and remains high until the termination of life, unless treatment controls the toxicity. The diastolic blood-pressure is usually low, giving a much increased pulse pressure.

Trophic symptoms occur as a brownish yellow pigmentation of the skin, thinning of the hair and longitudinal striae of the nails.

Mental disturbances are common in the late or very active cases and vary from a state of constant fear and apprehension to that of a decided psychosis.

2. Subjectively, the individual complains of nervousness, general weakness, palpitation, insomnia, pulsation in the ears when lying down, sweating of the hands and feet and, at times, general hyperidrosis. Frequently digestive disturbances occur, such as nausea, loss of appetite and diarrhea; menstrual irregularities in females; pain and pressure in the neck with a sensation of choking, or an irritable cough, and general feeling of "fag."

3. Laboratory calculations are most conclusive in the toxic state. Du Bois has standardized basal metabolism in the normal individual and Plummer has proven by extensive studies that thyroxin in excess raises the metabolic rate. Therefore, a sufficiently high metabolism is pathognomonic of thyroid hyperactivity and is one of its most important diagnostic features.

With hyperactivity of the thyroid, there is marked increase in cellular activity and carbon dioxid output, with a speedy demand for larger oxygen consumption. To determine the metabolic rate it is necessary only to measure the amount of oxygen consumed for a given period of time, and make calculations in calories per hour, by comparing the intake to certain physiological standards for body surface, temperature and barometric pressure.

Urinalysis reveals kidney changes in direct relation to cardiovascular degeneration and digestive disturbance. Scanty, high-colored urine signifies concentration due to evaporation and skin elimination. Albumen and casts are indicative of kidney dysfunction and contraction. The presence of sugar indicates diminished carbohydrate toleration.

The blood picture may reveal a decreased number of erythrocytes with lessened hemoglobin content or an increase in leucocytes with a larger percentage of lymphocytes and eosinophiles.

Blood chemistry shows an increase in blood sugar only, which is provided by the thyroid for an increased heat production. If the blood sugar rises slowly there is a compensatory function of the kidney that holds the balance, and there is no glycosuria. Should this tolerance be broken by increased carbohydrate ingestion, the kidney excretes sugar.

An editorial in *The Journal of the American Medical Association* for April 14, 1923 (page 1071) after discussing the roentgen rays and surgery in the treatment of exophthalmic goiter, says: "In the light of the present-day evidence, the choice of therapeutic procedure presents, indeed, a difficult perplexity."

We are positive that no one treatment will control all cases of toxic goiter, but

that after defining and correlating the symptoms and classifying the case pathologically, the indications for treatment should be manifest.

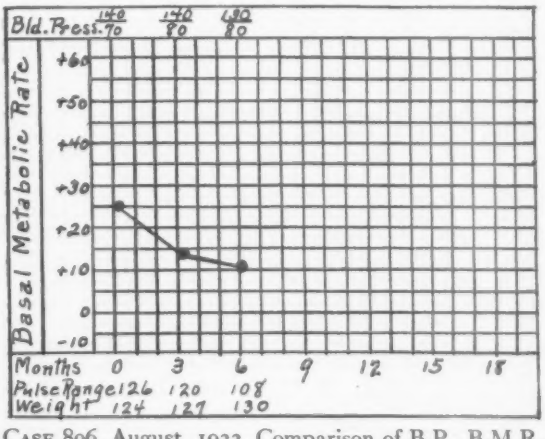
Furthermore, special consideration must be given to the associate or subsidiary symptoms before and after treatment. It is generally agreed that rest and quiet are helpful factors. An ice bag may be applied to the gland and precordium. Plenty of easily digested food, tepid baths and alkaline drinks are equally important. Digitalis as a therapeutic splint to an irregular, rapidly beating, dilated and decompensated heart, will sometimes tide over a catastrophe. Blood transfusion is indicated in a low cell count, 30 per cent or lower hemoglobin and general edema, and more especially when the toxemia has been profound enough to produce a severe psychosis. Bromides and ergot have their place in assisting in the control of certain symptoms.

It was through the efforts of the surgeon that we began to realize the importance of the present conception of the disease. For this reason, therefore, surgical findings in toxic goiter should be held in the highest regard.

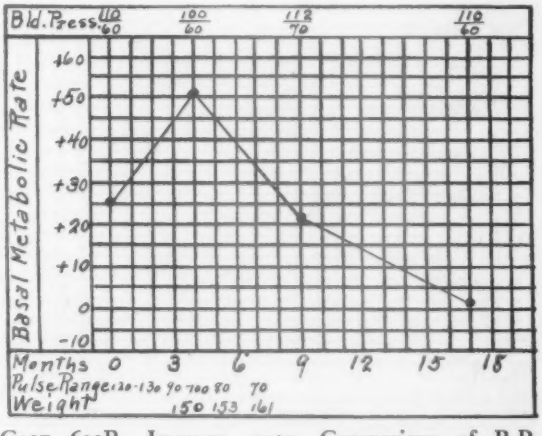
Without consideration of the surgical mortality in the most skilled clinics, we must consider this great danger in other centers; also the fear, apprehension, hospitalization and financial cost to the individual, not forgetting the possible return of all symptoms.

Leniency must be used in the criticism of scientific men who, ignoring radium entirely, assert that all treatments have failed except surgery. It must be remembered that prejudice and inexperience will warp the soul of the most sublime.

Radium therapy for toxic goiter as standardized and given to this Society by the author two years ago, at the Boston meeting, merits your serious interest. After seven years of experience with the element, the last three under the most exacting scrutiny by means of laboratory methods and clinical findings, I conclude that toxic goiter can be cured by radium and that it is *not* a surgical disease.



Case 806. August, 1922. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.



Case 603B. January, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.

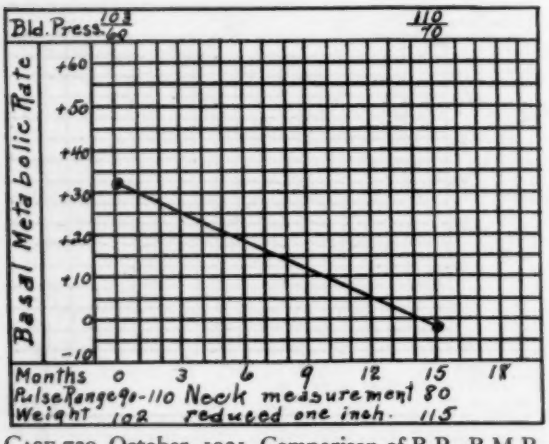
Of the 180 cases I have treated, only 10 were subjected to a second radiation. Four of these had large cystic adenomata and the toxic activity was not completely controlled after the first treatment. The other 6 were given the second treatment with the hope of further reducing the enlarged gland. Three cases, in a state of extremus from myocardial degeneration with general edema, died. One insane patient died from starvation before the treatment had time to benefit the toxemia.

Improvement is noted within the first ten days after treatment, but about the third week all the old symptoms may return, due to the radium reaction. This active stage varies in different individuals. Some express disappointment in not feeling

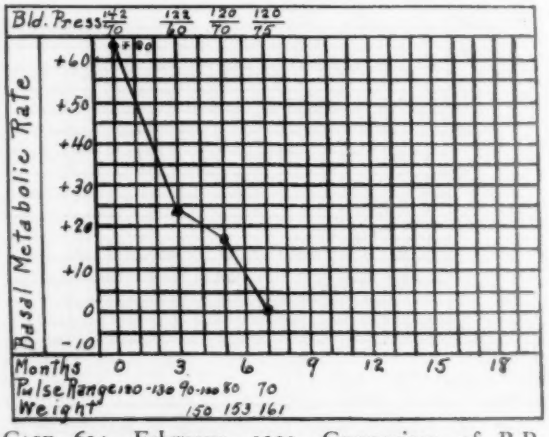
bad, while others are nauseated for a few days.

Within four weeks the nervous tremor has commenced to subside, the appetite has improved and the heart has slowed down twenty or thirty beats. After two months all the symptoms are much better and most individuals gain a few pounds in weight. The improvement is gradual, as shown by the cases reported when the metabolic rate has been taken every three months after treatment.

Some cases are free from all symptoms after six months, while others with large adenomata of long standing and with extensive myocardial change take twelve



CASE 720. October, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.



CASE 604. February, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.

to eighteen months to show a normal metabolic rate with a normal heart action.

The enlarged gland gradually decreases in size in direct relation to the amount of cystic formation present. All hypertrophy or hyperplasia is reduced to normal while the cystic type is reduced about one-half in size. The exophthalmus in many of my cases has been controlled after three years. However, all do not respond so favorably.

There has been no evidence of myxedema in any of the cases treated. Metabolic readings have been made over a period of two and a half years and all have remained normal.

Many toxic adenoma cases give a history of pregnancy, childbirth or miscarriage initiating the toxic activity. In these young women they run an active and rapid course, so that the symptoms are grave in a very few months. Sixteen of these cases have been treated, and 10 have had second and third pregnancies since treatment without any evidence of thyroid toxemia. Two showed activity at the beginning of lactation but were controlled by means of the ice bag.

Two of our cases had two operations each and 8 had one each for thyroidectomy. Four others had ligation of the thyroid arteries on one side and 2 had both superior thyroid arteries tied off. They had all been benefited for a period of six months to two years, but the remaining portion of the gland had hypertrophied and soon became active. On account of parathyroid glands, discretion in the technique of treatment of postoperative cases must be used.

None of my cases have shown any symptoms of parathyroid dysfunction after treatment.

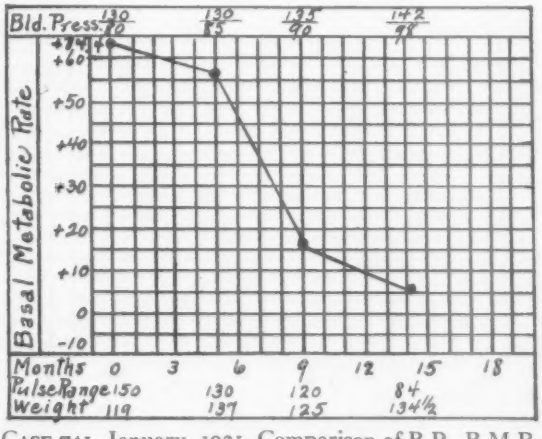
For the last two years all cases with infected tonsils associated with a toxic thyroid have received treatment over the tonsil area conjointly with that of the thyroid gland. One case had a gall-bladder drainage and two had operations for chronic appendix six months after the thyroid treatment.

Abdominal support is given all cases that show visceroptosis by roentgenography. It has been shown experimen-

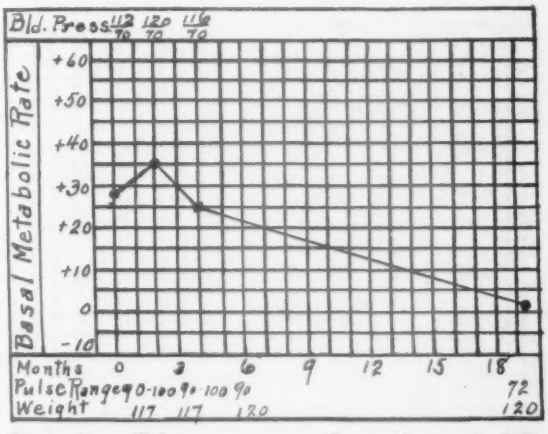
tally that stimulation of the cervical sympathetic nerves in animals produces exophthalmic goiter, and that thyroid secretions lower the threshold to sympathetic stimulation, so that a vicious circle is established.

It is a question whether radium therapy breaks the vicious circle by diminished gland secretion, thus restoring the balance by some specific effect of the rays on thyroxin itself, or whether radium acts mechanically by blocking the blood supply.

The rapid control of the toxic symptoms after treatment would support the hypothesis of a change in the character of the secretion. Diminished secretion due to



CASE 741. January, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.



CASE 611. February, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.

cellular change would come later, while thrombosis of the smaller arterioles and capillaries would come last of all.

Corroboration of the objective and subjective symptoms by laboratory standards will verify the findings and establish the diagnosis. The basal metabolic rate in thyroid toxicity proves more than clinical findings, as it registers the degree of severity as shown by the variation in records. A +60 case indicates greater activity, toxicity and severity than one of +20. This known difference in rate is a helpful factor in the prognosis of the case.

I wish to present here the comprehensive and forceful opinion of C. F. McClintic, M.D., Professor of Anatomy, Detroit College of Medicine, explaining many of the anatomical changes and physiological dystrophies of the thyroid toxemia.

SIGNS AND SYMPTOMS IN EXOPHTHALMIC GOITER

It certainly must be more than a mere coincidence that the signs in exophthalmos so closely approximate the phenomena which result from the experimental stimulation of the inferior sympathetic cervical ganglia. These signs have been produced in dogs and have also been observed singly or in combination in man when these ganglia were stimulated or irritated.

Let us notice, therefore, the anatomical and physiological mechanisms associated with these ganglia and their accompanying phenomena.

1. There is a sheet of involuntary muscle in the upper lid which is supplied by filaments from the cervical ganglia. When this muscle (Mueller's) is stimulated to contraction the upper lid becomes narrowed, the lid rises above the upper margin of the cornea and exposes the white sclera and results in a widening of the palpebral fissure. This accounts for the signs of Graefe and Stellwag.

2. Stretched across the sphenoidal fissure in the apex of the orbital cavity is a sheet of involuntary muscle, the orbicularis muscle, which is supplied by sympathetic nerves from the above ganglia. When this muscle contracts it pushes forward the contents of Tenon's capsule and thereby causes protrusion of the eyeball, or exophthalmos.

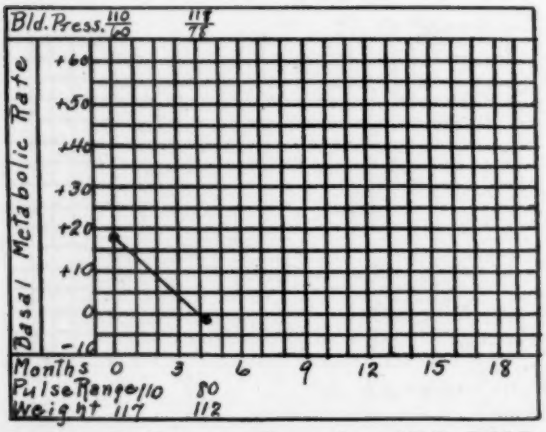
3. In the orbicularis oculi and musculature of the forehead are strands of involuntary muscle which, when stimulated, prevent wrinkling of the skin of the forehead. This musculature is supplied by the sympathetic ganglia of the neck. This mechanism explains Joffroy's sign.

4. (*a*) From these ganglia arise the accelerator nerves to the heart; their stimulation therefore increases the force and rate of the heart tachycardia, and thus raises the blood-pressure.

(*b*) The disturbance of the heart and vasomotor centers assists in explaining the gastro-intestinal and toxic symptoms.

5. The sympathetic nerve when stimulated increases the capacity of the respiratory tree, and the chest remains full (therefore expansion is more limited). This increase in lung capacity with the circulatory changes will explain the findings in basal metabolism.

6. The vasomotor nerves to the head, face, neck and upper limbs arise from these ganglia and thereby account for sweating and other vasomotor phenomena. It has been



CASE 833. October, 1922. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.

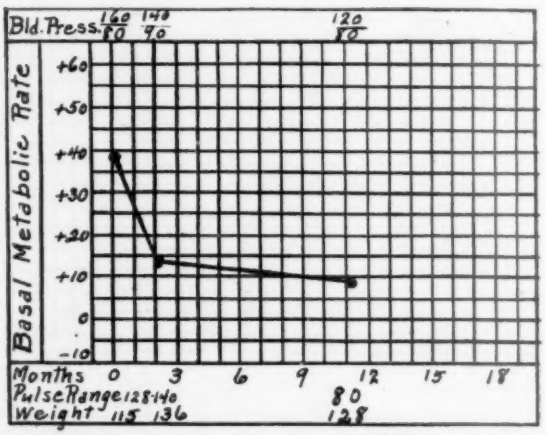
demonstrated experimentally, that these areas are intimately connected with those of the lower extremity.

7. The tremor and rhythm are the same as those for smooth muscle. Langley has shown that all voluntary muscle is supplied by the sympathetic. This will explain how the irritation of these ganglia will account for the tremor. It also explains the sign of Moebius.

8. The bruit associated with exophthalmos and enlarged thyroid is accounted for by the relations of the gland to the common carotid artery. The enlarged gland presses upon and constricts the lumen of the vessel. The blood rushing through the narrowed lumen into the larger portion produces the bruit.

9. The pulsation of the gland may be due to increase in the flow of blood through the inferior thyroid arteries since the gland acts as a shunt to prevent too much blood reaching the brain. It is interesting to note in this connection that filaments of the sympathetic encircle the inferior thyroid artery. When, for any reason, the diameter of the artery becomes increased it tugs upon the nerve and thereby irritates the ganglion, the irritation stimulates the ganglion, it in turn stimulates the heart to force more blood through the artery, this again increases the tugging on the ganglion, etc., thus initiating a vicious circle which can produce all the signs of the condition. May this not account for Osler's cases which occurred from fright and soon passed off?

10. Changes in the gland may occur as a result of the disturbance of its nutritional mechanism. The disturbances or irritation of the ganglia may result from (*a*) pressure due to enlargement of the thyroid gland, (*b*) increase in the diameter of the inferior thyroid



CASE 687. July, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.

artery, (*c*) from infections in the neck or pharyngeal regions, (*d*) due to toxins showing affinity for the thyroid circulation. (Wm. J. Mayo has called attention to the specificity of certain circulatory areas for certain strains of bacteria.) (*e*) General disturbances of the sympathetic nervous system from toxins, faulty diet, emotional states, etc.

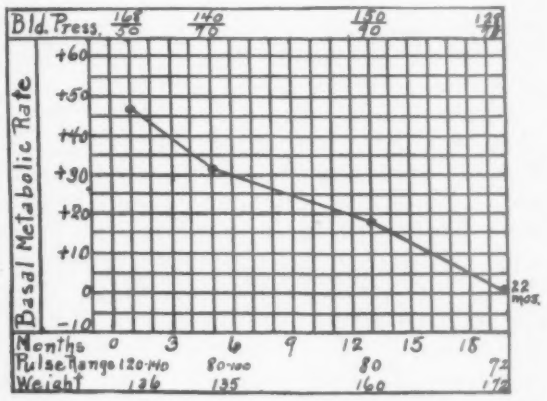
11. Fitting in with these facts is the adrenalin test for exophthalmic goiter. It is to be expected that the administration of adrenalin will aggravate all of the above-mentioned phenomena.

The writer merely mentions these facts as a possible explanation for the signs in exophthalmic goiter based on the functional mechanism associated with the cervical sympathetic ganglia.

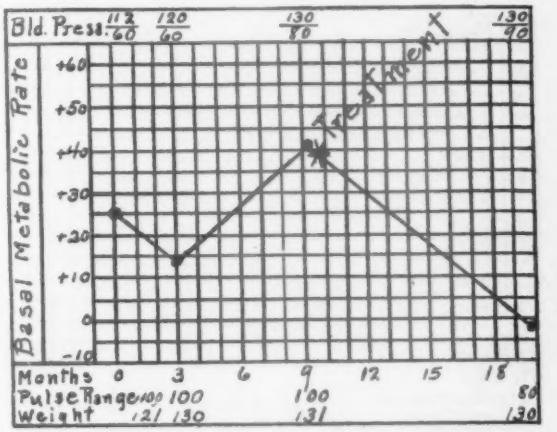
RADIUM TREATMENT

At least 100 mgm. of element are used (more often I use 130) in four tubes, each tube being screened in one mm. of brass and 1 mm. of gum rubber. To obtain distance, the screened tubes are placed 1 cm. apart on a gauze pad 2 cm. in thickness.

The gauze pad is made with a loop of adhesive tape at each end so that it can be adapted and tied over an unevem surface without strapping. The radium pad is placed over one lobe for eight or ten hours and then over the other for an equal time, depending on the size of the lobe and the amount of radium used. If the isthmus is enlarged the pad can be arranged to cover one side of it at each application without overlapping and endangering the trachea.



CASE 599. January, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.



CASE 726. January, 1921. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.

This technique in treatment will give an active hyperemia in the blonde type of individual. The susceptibility of some people (especially if there is a vasomotor disturbance like sweating) has to be considered; so that judgment must always be used at all times.

It is well to advise the use of the ice bag in hourly periods each day, over the gland, for a few weeks following the treatment. This insures rest and controls circulatory and cellular activity. As mentioned before, subsidiary treatment is important after radiation to control arising symptoms of insomnia, tachycardia, indigestion, diarrhea, etc., until the therapeutic effect of the radium has been established.

CASE 726. Jan. 29, 1921. Female, aged thirty-one years; married; mother of one child eight years of age.

Family History. Negative.

Past History. Had measles and smallpox when a child. Menstruated at thirteen years; always regular. Had a left brachial cyst removed when seventeen, also had tonsillectomy. Had an ovarian cyst removed five years ago. For the last two years she has had "throat trouble." Had difficulty in breathing and, when going up stairs, tracheal pressure. Severe headaches; fatigue and disinclination to work. Perspires freely and at times has one or two degrees of fever. Appetite good; bowels regular; no insomnia. Has had some middle-ear disturbance from Eustachian infection.

Examination. No eye manifestations. Fragments of lymphoid tissue within the pillars of both tonsils so that the posterior pillars are adherent to the pharyngeal walls and show evidence of infection. The thyroid gland is enlarged; not cystic, but soft, and causing a compression of the trachea. The left lobe extends beyond the sternomastoid muscle and adjoins the brachial cyst keloid scar. The right is also enlarged but lies well behind the muscle. The area of heart dulness is normal in outline and no murmurs are detected. Pulse rate 110; blood-pressure: systolic 130, diastolic 80. Metabolic rate plus

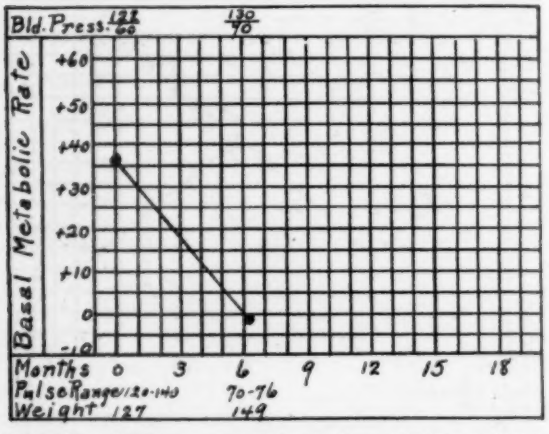
24.1. Upper circumference of neck 13¾; middle 14¼; lower 14¾ in. There is a tremor of fingers on extension; nails have longitudinal striae.

Diagnosis. Toxic adenoma.

Treatment. Local treatment for throat; rest; ice bag to neck with quinine hydrobromid medication.

April 23, 1921. Throat much better, with some improvement in general symptoms. Metabolic rate today plus 13.5.

Oct. 7, 1921. Improvement was only temporary, so that now all the symptoms are exaggerated. Headaches worse; tachycardia; pulse 120; some diarrhea. Metabolic rate plus 40.4. Recommended radium treatment.



CASE 810. August, 1922. Comparison of B.P., B.M.R., pulse range and weight in months after radium treatment.

Nov. 2, 1921. One hundred mgm. radium element were used with previously described technique over each lobe of the thyroid for ten hours, and 40 mgm. in the same screening held behind the jaw over each tonsil area for ten hours.

The patient made a satisfactory recovery with complete alleviation of all symptoms. She moved to another city so that I was unable to follow the course of the improvement.

Dec. 7, 1922. After fourteen months of complete relief from all the old symptoms the scar on the side of the neck has softened down and both lobes of the thyroid are apparently normal in size. The lymphoid tissue at the site of the right tonsil has disappeared and the left is healthy in appearance. Pulse rate 80; full and regular. Systolic blood pressure 122; diastolic 80; metabolic rate minus 2.1.

CASE 810. Aug. 11, 1922. Male, aged thirty-nine years; married; brakeman. Complained of shaking of the hands, legs and body and of fatigue.

Family History. Negative.

Past History. When thirty years of age he had a renal colic and passed a calculus. Two years ago he was in a railroad accident and had his left clavicle and three ribs broken, also both shoulders injured. He was laid up for five weeks and was very nervous for three months following. About a year ago he had influenza.

Present Illness. Three months ago he became shaky in the limbs, weak, tired easily, was nervous, had insomnia and would wake after sleep with a feeling of fulness in his head. Would almost faint at times from weakness and palpitation.

Examination. Right eye slightly larger than the left. No other eye symptoms. Tongue tremulous. Both tonsils enlarged and chronically infected. Tonsil crypts were filled with necrotic material. Throat and soft palate injected from smoking. Teeth in good condition. Neck very slightly enlarged. Left lobe of thyroid larger than right. Isthmus normal. Some pulsation in neck but no bruit heard. Heart dilated with apex in nipple line. Heart sounds rapid, but no murmur detected. Tremor of hands and knees. Nails have longitudinal striae. Radial pulse 100; apex beat 120; systolic blood pressure 122; diastolic 90; metabolic rate, plus 36.1.

Diagnosis. Primary exophthalmic goiter.

Prognosis. Good; should be controled.

Treatment. (1) 60 mgm. radium element in 1 mm. brass and 1 mm. rubber and 1½ cm. gauze was held beneath right ear over tonsil area for seven hours. (2) 100 mgm. in 1 mm. brass, 1 mm. rubber and 2 cm. gauze in form of a pad was held over left lobe of thyroid for seven hours. (3) The same packages were held over the right tonsil area and thyroid lobe for eight hours.

Sept. 14, 1922. Present weight 133 lbs., or a gain of 6 lbs. since August 11th. Has been feeling fine. Complains of some

palpitation and precordial heaving after eating and vigorous exercise. Has had no sore throat or distress of any kind; toxic symptoms lessened greatly.

Examination. Throat and mouth still injected from smoking. Tonsils small with some infection in the left one; neck not enlarged. Heart sounds normal. Pulse and apex beat 100. Systolic blood pressure 130; diastolic 60; metabolism not taken.

Feb. 12, 1923. The patient was treated six months ago. Has never felt better in his life; complains of rapidity of heart action on exertion only. Examination showed the eyes normal; color good; neck still small with no evidence of enlargement or local effect of treatment. No tremor; all symptoms controled. Present weight 149 lbs., or a total gain of 22 lbs. Pulse rate 74; systolic blood-pressure 130; diastolic 70. Metabolic rate minus 3.9.

CASE 805. July 13, 1922. Female, aged thirty-nine years; married; housewife. Complained of choking sensation and general weakness.

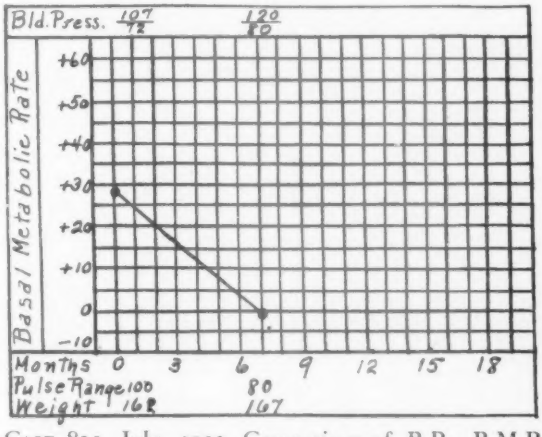
Family History. Negative, except that her mother had goiter.

Past History. Had children's diseases. Always been more or less anemic. At the age of six years the thyroid gland enlarged but became smaller after puberty. Gave no evidence of activity until after the birth of her first child. When lactation ceased the activity subsided until after her second child was born. The activity persisted this time and she was compelled to have a complete left, and a partial right, lobectomy performed three years ago. All symptoms subsided and she remained well for over a year. The gland commenced to enlarge gradually but without any symptoms until about a month ago when she had an acute attack of tonsillitis.

Present History. The patient finds it difficult to breathe at night when lying down, so has been compelled to sleep in a sitting position for nearly three weeks. Has a choking sensation in stooping over or on exertion. Is weak, fatigues easily and is disinclined to work.

Examination. Left eye full and more staring than the right. Right eye also prominent but shows less sclera than the left. Both tonsils enlarged, injected and appear infected. The tongue is tremulous. The neck shows a circular scar down near the clavicle with a bulging prominent right lobe of the thyroid, and an enlarged cystic isthmus. The mass as a whole forces the trachea toward the left and holds it backward, accounting for the choking sensation with increased blood pressure in the head. Upper circumference of the neck is 15 in., middle 15½, lower 16. Heart sounds normal; no murmurs detected. Apex beat and pulse registering 90; systolic blood pressure 107; diastolic 72; hemoglobin 65 per cent; metabolic rate plus 29.0. Some tremor of the hands and fingers.

Diagnosis. Toxic adenoma, recurring as a result of acute tonsillar infection.



CASE 805. July, 1922. Comparison of B.P., B.M.R. pulse range and weight in months after radium treatment.

Treatment. Ninety mgm. radium element in four tubes screened as before, made into a pad 2 cm. in thickness and held over the right lobe and isthmus for twelve hours. Eighty mgm. in two packages of 40 mgm. each with same screening was held below the ear and behind the jaw over the tonsil areas on each side for ten hours.

Feb. 3, 1923. It has been nearly six months since the treatment. The patient reports that within a month she began to improve and that now she feels well; has no nervous symptoms, choking spells or other discomfort.

Examination. Patient looks much better. Right eye still full; right tonsil small; left red and injected. Right lobe and isthmus smaller and measurements show a decrease of 1 in. in each of the two upper

circumferences, and 1½ in the lower. Gland soft, and very little tension in the cystic isthmus. The pulse rate is 78; systolic blood pressure 112; diastolic 80; hemoglobin 85 per cent; metabolic rate minus 2.2. The patient has gained 3½ lbs. in weight.

May 16, 1923. At the present time there is no evidence of thyroid toxicity except the fulness of one eye; and the patient reports feeling very well with none of her old symptoms present.

CONCLUSIONS

1. A high systolic and a low diastolic blood pressure show a normally balanced pulse pressure in some cases before the metabolic rate becomes normal.

2. Three months after treatment the metabolic rate was found to be normal in many cases that had been active.

3. A high systolic blood pressure in the late stages of a toxic adenoma is conclusive evidence of myocardial or renal degeneration whenever it is not reduced 20 or 30 per cent after the normal metabolic rate has been re-established.

4. The basal metabolic rate proves and estimates the degree of thyroid activity and also furnishes conclusive evidence of toxic control after radium therapy.

CERTAIN BIOLOGICAL PRINCIPLES OF RADIATION THERAPY*

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TIME is all too short to give the résumé of this subject that had been contemplated. We shall, therefore, be content to present certain important fundamental principles of radiation therapy, divided for logical discussion into three chapters, depending upon whether the phenomena bear upon the physical, histological or clinical aspects of the cases treated.

This will necessitate making broad statements, to which possible exception may be taken, but will in general present the working ideas that we hold in the treatment of neoplastic conditions by gamma and *x*-rays.

I. PHYSICAL PHENOMENA CONTROLLING THE REACTION TO RADIATION

Let us consider briefly what happens when a beam of gamma or *x*-rays passes through any material substance. We know that the greater the density of the screen the more radiation there is absorbed; and it has been proved that the greater the amount of radiation stopped or scattered the more intense is the local ionization yielded through the production of negative electrons—secondary beta particles (the so-called delta rays). These are in every way comparable to soft beta radiation.

The stimulus afforded by the various types of radiation may be detrimental or beneficial to biologic function, the outcome depending largely upon the dosage, that is, the duration of exposure. For example, a certain radiation acting for a brief time on sugar cane may not only facilitate growth but also produce an increase in the sugar content of the stalk of cane (Burns[1]). If, however, this optimum amount of radiation is overstepped, the plant being submitted to a longer exposure or to a greater concentration of rays, there is produced depression, culminating in complete arrest of physiologic function.

The profound retrogressive changes produced by rays of radium on tissue cells are well known. The explanation for this phase of the reaction has been varied. Some investigators have reached the conclusion that the growth-promoting factors in cells can be inactivated by exposure to radiation; and the therapeutic usefulness of radium in checking the cell growth may be ascribed to such a destructive reaction. This factor, the retardation of cell multi-

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plication, has been proved to be transmitted as a mendelian character; not only from cell to cell (Wood and Prime[2]) but from parent to the offspring in mammals (Bagg[3]).

According to other observations, however, the growth retardation may be due to the increase in the permeability of the cells by the injury done to the cell walls through ionization. If treatment is continued, the cells cytolyze completely (Packard[4]). From this it follows that when cells are already highly permeable, as they are during growth and division, complete cytolysis quickly ensues; whereas, when the cell membrane is relatively impermeable, as in the resting condition, radiation must be long continued before destructive cytolysis can be observed. In this connection it will be apparent that those cells in particular which contain electrolytes and substances of high atomic weight will show a greater degree of radiosensitiveness.

It is, therefore, probable that the direct effect of the incident beam of gamma or *x*-rays is practically *nil* and that the biological effect depends almost, if not entirely, upon the amount of ionization produced within the tissues, which, as we have seen, is a function of the absorption and scattering coefficients.

We do not mean to state that the secondary beta particles will all produce the same biological effect; in fact we are, from theoretical considerations, opposed to this view, for it seems evident that the speed of the delta particles (and hence the energy and ionizing power) must vary through certain limits with the amplitude of the incident primary beam (Proust[5]).

II. STRUCTURAL CHARACTERISTICS (HISTOLOGICAL) WHICH DETERMINE THE REACTION TO RADIATION

Regardless of their future as therapeutic agents the use of radium and *x*-rays has demonstrated certain hitherto unknown cellular characteristics (Ewing[6]).

It was observed that certain tissues were *resistant* to even large doses of radiation while others were quite *susceptible* and underwent resolution or retrogression with remarkably small units of beta, gamma or *x*-rays. In general, there are six structural characters which determine susceptibility to radiation. All are of a cellular nature (Withers[7]):

(*a*) It has been shown that the more embryonal or undifferentiated the type of cell the greater is its radio-susceptibility; and conversely the more differentiated, highly specialized the type of cell the greater is its radio-resistance, in general (law of Bergonie and Tribondeau).

(*b*) It is easily demonstrated that cells in the process of dividing (mitosis) are from eight to fifteen times more vulnerable to radiation than when in the resting condition (Mottram[8]). The radio-sensibility too, is a property of the nucleus and is inherent in certain states or temporary physiological periods of cell life, the most important and best known of which is the state of reproduction (Regaud[9]).

(*c*) It is equally true that cells containing large amounts of chromatin material are more easily killed than those containing little chromatin. In other words, cells having hyperchromatic nuclei are in general much more radio-sensitive than similar cells having small amounts of chromatin in the nucleus.

(*d*) It is common knowledge that the endothelium of blood and lymph vessels is very radio-sensitive and that tumors having an abundance of thin-walled, delicate capillaries react much more quickly and favorably to radiation than corresponding tumors having a scanty blood supply.

(*e*) Tumors having small amounts of intercellular connective tissue react much more quickly and favorably to radiation than new growths having an abundant stroma.

(*f*) A period of heightened sensibility corresponds to the maximum metabolic activity of the nucleus in cells which have a secretory function (Regaud[9]). In general it may be said that cells which secrete crystalloid or crystallizable material are much more radio-sensitive than non-secreting cells having the same histological characteristics, or cells that secrete colloid or protein substances.

It was the presence of these histological characteristics, wholly or in part, in tumors which responded quickly to radiation, that led certain authors to assert that radium was selective in its action for certain types of cells.

The effect on the cell is shown by every degree of change from stimulation to death. The dead cells are removed by autolysis and phagocytosis, but the connective tissue substances are resistant and they are absorbed slowly. Arguing from these premises Regaud asserts that gamma and *x*-rays of very short wave-length are "elective-poisons" for nuclear chromatin, upon which, as is known, heredity depends. Hence the rays suppress or suspend cellular reproduction in a tissue.

On the other hand, tissues prove relatively insusceptible to radiation when the cells are differentiated, adult in structure and contain small amounts of chromatin in the nucleus; when they grow slowly and mitoses are few; when the blood supply is through well-formed, adult vessels and when there is much intercellular material or stroma (Ewing[6]).

Again, the presence or absence of any one of these characteristics to a marked degree enables one to predict on *a priori* grounds that the growth *will* or *will not* retrogress favorably under radiation properly applied. The radio-sensibility of cells does not in anyway depend upon the anatomical location, but entirely upon the histological picture presented.

For example a lymphoid hyperplasia which is made up of hyperchromatic and undifferentiated cells is almost as vulnerable to radiation as sex cells and will undergo retrogression with mild radiation whether it be a lymphosarcoma, a Hodgkin's gland, an hypertrophied Peyer's patch, a thymic or tonsillar hypertrophy or a tuberculous cervical adenitis.

III. CLINICAL CONDITIONS WHICH INFLUENCE THE REACTION TO RADIATION

The clinical conditions which influence the reaction to radiation may be divided into two groups: those purely local in their manifestations and those of a constitutional nature.

1. Local Conditions Which Influence the Reaction to Radiation. (*a*) One of the most important reactions following the irradiation of a localized area is the intense infiltration of cells and serum which accompanies the inflammatory reaction. The presence of this zone of lymphocytes and plasma cells constitutes the first barrier to the neoplastic invasion, just as the leucocytic infiltration about a pyogenic infection walls it off. It has been very well proved by Broders[10] and others that the presence of a round-cell infiltration in the zone of proliferation of an uninfected malignancy argues that such a growth is relatively less malignant than one having a similar cell structure, but without the intense round-cell infiltration. In other words, the presence of a round-cell infiltration about a malignancy, whether it occurs as a part of the natural body resistance, or is stimulated by radiation, is one of the first steps in causing the retrogression of neoplastic elements.

(*b*) The study of the vascular connective tissue of the stroma has furnished us with data which deserves to be emphasized. In the biopsies practiced before treatment, the characteristics observed almost always in patients in whom a favorable outcome of the course of treatment can be expected (Laborde[13]) are as follows: A connective tissue stroma of normal appearance with a minimum of acute inflammatory reaction, a collagen woof taking a normal stain, the presence of capillaries, of which the walls appear well formed, the occurrence of perivascular infiltration of round cells and polynuclear eosinophiles.

On the contrary, the aspects which have appeared unfavorable to us, from the point of view of the local reaction upon the stroma of the tumor, as well as that of the resistance of the stroma to radiation, are a dissociated connective tissue, whose fibrils have more or less lost their affinity for stain, or vessels, the walls of which appear altered, and an infiltration of the polynuclear neutrophile type only.

As a result of these researches, it is evident that the condition of the vascular and connective tissue stroma deserves further study, not only in the course of treatment by radium, as has been done by

most writers up to the present, but also and particularly *before* treatment. The perivascular alterations which we have observed in some cases before a therapeutic treatment prove that there is an undeniable interaction of neoplasm on the stroma and explain to us why, in certain cases, the alterations of vascular and connective tissues are much more pronounced in the course of some treatments than in others.

(*c*) The repair of irradiated tissue following the radiation reaction is brought about through the deposit of white fibrous connective tissue in interlacing lamellae throughout the area radiated. This scar tissue formation is similar to the repair that takes place in other traumatized areas, and is a function of the absorbed radiation and largely due to the secondary beta particles, as before mentioned.

(*d*) Accompanying the irradiation is produced a local obliterative endarteritis, which in many sections has the appearance of marked arteriosclerosis. This closing of the blood-vessels and lymph spaces through the combined action of the arteritis, perivascular round-cell infiltration and scar tissue formation, effectively incarcerates persistent neoplastic elements.

(*e*) Regaud[9] points out that when an area is subjected to repeated doses, the same normal cells are irradiated, but not the same malignant cells. Hence the integuments and connective tissue elements become successively *less* radio-resistant through the cumulative changes which have made the malignant cells become *more* radio-resistant. And in those cases where a cure, and not palliation alone, is sought, an attempt should be made to give the entire dose at a single sitting, to avoid the necessity of giving a second or third dose of greater intensity with the consequent greater damage to normal elements.

2. *Constitutional Conditions Which Influence the Radiation Reaction.* These conditions can be summed up by saying that any condition which affects the body as a whole must necessarily affect every cell in it. Please understand then, that when dealing with malignancies it is necessary to have the physical functions of the body as nearly normal as possible. The presence of a marked cachexia with the usual anemia and leucopenia should make the prognosis guarded even though the malignancy is well localized and one which would ordinarily be termed favorable. This is likewise true in the case of diabetics or luetics and those having marked cardio-vascular or cardio-respiratory diseases. The presence, then, of any marked constitutional disability seems to render the normal tissue more radio-susceptible and the repair following irradiation prolonged in the extreme. Without wishing to be dogmatic there is some reason for believing that patients showing little lymphocytic fall in the circulating blood upon irradiation react better to the treatment than those in which a marked fall occurs (Lazarus-Barlow[11]).

On the other hand, constitutionally important phenomena are known; in particular, the modifications of the blood which follow the treatment of cancer by penetrating rays. According to Seitz and Wintz, the alterations of the blood are constant and characterized by an abundant destruction of the formed elements. In general, it takes from six to eight weeks for the blood to return to the condition which existed before irradiation. Certain patients cannot regenerate their blood-cells, and when the sanguinary alterations continue, they die, the strong doses of ray seeming to have hastened their death.

In addition there are certain changes produced in the organism which are the direct result of the irradiation upon neoplastic cells. We refer to the production of substances formed under the influence of the irradiation which may act in the manner of antibodies. Contamin has shown that the inoculation of mouse or rat tumors feebly irradiated produces an immunity against additional grafts of the neoplastic tissues. It is necessary here that the irradiation should be just sufficient to produce an inhibition of the neoplastic elements, because if the dose is too large, inoculation of the irradiated tumor is no longer capable of conferring immunity. These experiments have been repeated quite recently by H. Charles, G. Scott and Sidney Russ[12] and have con-

firmed the possibility of conveying immunity by neoplastic grafts. It seems true that immunity cannot be produced by inoculation of cells which are still living. On the other hand, it is well proven that the indirect action on the cancer through antibody formation is insufficient to inhibit its growth, and the actual state of our knowledge at present is that we do not know how to provoke this reaction. According to those who are best informed, we can count only on the local action of the rays. It is therefore essential that all the neoplastic cells of a tumor receive sufficient doses of rays to bring about their destruction, because not only can the incompletely irradiated elements become a point of growth departure for a recidive, but weak doses are likely to provoke a stimulating reaction. With these conditions it is advisable that proper measures be taken to promote body welfare, and that irradiation be undertaken with a great deal of thought and preparation so as not to hurry such patients to their death by over-irradiation.

In the practical treatment of malignancies with radium or *x*-ray there are four chief points to be kept in mind which necessitate the very closest cooperation of the surgeon, pathologist and radiation therapist:

1. The pathology must be interpreted into terms of radio-sensitiveness.

2. The proper area or areas for irradiation must be accurately determined.

3. The required dose of radiation must be placed in that part of the growth where the active proliferation is taking place to stimulate normal tissue resistance to the invading neoplasia and obliterate the blood-vessels and lymph spaces.

4. The normal tissues must be protected in every way possible so as not to break down the natural body resistance through the destruction of continuity of normal tissue stroma, intra- and peri-tumoral cellular infiltration, and the formed elements of the blood, which make up the triumvirate of tissue defenders. These must be conserved and stimulated.

Reactions to radiation are not only qualitative but quantitative, when all the factors involved are taken into consideration; but this statement does not permit of the interpretation that there is, or can ever be established, a standard carcinoma or sarcoma dose, since no two growths have identically the same cell structure or surrounding normal tissue stroma permitting identical reaction.

CONCLUSIONS

1. That the cellular reaction to radiation depends upon the amount of radiant energy absorbed, whether it be primary or secondary in origin.

2. That susceptibility to short wavelength therapy is a cellular characteristic depending upon a definite histological structure.

3. That the normal tissue reaction to radiation and neoplastic invasion depends to a large degree upon the well-being of the body as a whole.

4. That there is sufficient data extant to predicate on *a priori* grounds those tissues or tumors which will prove radio-resistant or radio-susceptible.

5. That the use of radium or *x*-rays is just as radical and rational a procedure as the use of other physical agents in the treatment of neoplastic conditions.

6. That the use of radium or *x*-rays in a given condition should require also an equal amount of surgical judgment, a more complete knowledge of the pathology present and a broader biophysical training than the corresponding surgical treatment demands.

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A STUDY OF THE ACTION OF MEASURED RADIATION DOSES ON CARCINOMATA OF THE UTERINE CERVIX*

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IN the radiation treatment of carcinoma of the uterine cervix, clinical and microscopic examinations are of the utmost value for diagnosis, prognosis and treatment. The effectiveness of the radiation depends on the radiation energy applied, the extent of the disease within the true pelvis, the type of epithelial cell composing the new growth and the constitutional reaction caused by the effects of radiation. We must render the prognosis and determine the method of treatment solely from these findings.

A study of the cervical carcinomata from this viewpoint has been undertaken to ascertain whether the lethal radiation doses for the different types of cells found in these new growths could be determined.

As early as 1904 Exner[1] described the changes caused by radium rays in a breast cancer. He attributed to the connective tissue the greatest importance in the dissolution of the malignant growth. Additional similar investigations were reported by Caan,[2] Finzi,[3] Janeway,[4] Wickham and Degrais,[5] Ewing,[6] Bumm, Doederlein, Weinbrenner,[7] Kelly and Burnam,[8] Kehrer,[9] Lahm[10], Clark, J. G.,[12] Schmitz,[13] Alter[14] and others. Lahm[10] asserted that the changes in the connective tissue are secondary, while those in the cancer cells are of primary importance.

Carcinomata of the uterine cervix are composed of either basal, squamous, or cylindrical epithelial cells. The greater the degree of immaturity, of departure from the adult normal histological type, the greater is the clinical malignancy. The basal cells are spindle-shaped and unripe and have not as yet acquired the differentiated adult form of either the squamous or the cylindrical epithelial cells. Therefore the basal-cell cervical carcinomata are the most malignant. Cervical carcinomata are seen as proliferating, ulcerating or infiltrating growths. Adams and McCrae state that all cases are carcinomatous in which there is infiltration and apparently independent growth of epithelial or gland cells into the surrounding tissue; and this, whether of slightly or markedly atypical cells.

Repeated cervical lacerations disturb the normal structures and functions of this tissue, interfere with its nutrition and expose the weakened structure to chronic irritation and inflammation. A chronic endocervicitis precedes cancer in the great majority of cases—34 out of 48 (Polese). The routine examination of this tissue may reveal abnormalities in the morphology and position of the epithelium which constitute precancerous conditions. The most prominent of these conditions is the cervical erosion, many instances of which show suspicious hypertrophy and heterotopia of the lining epithelium. Beckmann saw the development of carcinoma in an erosion which he had treated for five years (Ewing). Carcinomata do not primarily develop in the scars resulting from the healing of lacerations from the trauma of labor.

The changes produced by radium and *x*-rays in carcinomata concern those seen in the parenchyma and those observed in the

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stroma. The carcinoma cells undergo degeneration and the connective tissue cells and blood-vessels of the stroma show signs of inflammatory reaction.

The degenerative changes of the cells are chiefly a necrobiosis of the nucleus which leads to a complete breaking up or caryolysis. The ultimate fate of the cell is thus settled.

The inflammatory reaction begins soon after the radiation and consists of an infiltration of the stroma with polymorphonuclear leucocytes, at first without a proliferation of the stroma cells and blood and lymph vessels. Many of the cancer cells are densely surrounded by leucocytes, and one gains the impression that substances are liberated by the disintegration of the cells which exert a pronounced chemotaxis on the leucocytes.

At times, here and there in a section, are seen remnants of carcinoma cells, which impress one as being almost entirely composed of a leucocytic exudate. However, on closer examination blood-vessels with necrotic walls and thrombi are seen; and this contradicts the latter deduction.

The changes seen in the blood-vessels within the tumor consist mainly of thromboses and inflammatory processes in the walls resulting in an obliteration of the lumen and necrosis of the surrounding tissue. Changes in the cells of the connective tissue are not seen in the early stages. However as time passes we observe a rapidly increasing formation of fibroblasts with a corresponding decrease in the number of polymorphonuclear leucocytes. The latter are replaced with lymphocytes and plasma cells. Finally is seen the formation of connective tissue fibers, which gradually increase in numbers. Therewith the changes in the carcinoma tumor are completed.

We do not wish to state whether the changes in the parenchyma or those in the stroma are primary and most important.

In 1917 in a paper read at the annual meeting of the American Radium Society we called attention to the difference in the changes produced by radium in the different types of carcinoma cells as follows:

The squamous-cell carcinoma of the cervix evinces a papillary arrangement of the cells. Hornification or epithelial pearl formation is often seen. The connective tissue is edematous and loose. The round-cell infiltration in the wall of defense consists of plasma cells, eosinophiles, mast-cells, leucocytes and lymphocytes. It is mostly an everting, rapidly proliferating cancer without simultaneous extension into the tissue.

The changes caused by radiations in the epithelial cells of the epithelioma are cytolysis and caryolysis as granulation and vacuolation of the protoplasma, destruction of the cell wall, loss of staining power of the nucleus, cessation of mitosis and breaking up of the nucleus into amorphous debris. As the disintegration of the carcinoma cells progresses, so the round-cell infiltration and fibroblast formation increase. The round-cell infiltration is especially rich in eosinophiles. The tumor disappears by the action of phagocytes.

The unripe basal-cell carcinoma of the cervix shows columnar arrangement of the spindle-shaped cells with very little connective tissue. The growth is mostly infiltrating. The rays cause a necrosis of the central portion of the alveoli characterized by the formation of amorphous masses and cell detritus, while the peripheral cells are the last to succumb. Giant-cell formation is almost always seen. The vacancies in the tumor are rapidly filled by fibroblasts. Necrosis and connective-tissue formation are the characteristic degenerative and reparative processes in this variety of carcinoma.

The cylindrical-cell carcinoma usually shows an adenomatous arrangement of an acinous type. The connective-tissue stroma between the adenomatous masses of cancer cells is more or less prominent. A wall of round cells is usually present. The rays cause a rapid degeneration of the carcinoma cells with a corresponding rapid formation of fibroblasts.

Alter,[14,15] in a valuable study, discusses the histological changes of the different cell types of carcinoma after exposure to radium rays. He investigated the mechanism of the changes separately in each individual type of epithelial cell cancers. By comparison of the change

in the parenchyma and the connective tissue of each type he answered the question: Is the connective tissue proliferation or the change in the parenchyma primary? In passing I might state that Alter saw a very marked eosinophilia in most of the microscopic sections examined. The varying clinical response of different types of malignant disease to radium must impress even the most causal observer. These differences appear to be correlated to variations in the histological character of the growth. Both the nucleus and the protoplasm figure conspicuously in the histological changes following exposure to the rays of radium. Both these parts of the cell show different behavior toward the rays in the different types of carcinoma. These differences suggest different absorption of the rays. The physiological action of the rays is proportionate to the absorbed amount, but will also depend upon the kind of process initiated through the transformation of absorbed energy. The protoplasm of the benign and of the different types of malignant cells reacts differently toward the rays. This difference suggests again that different physical-chemical and chemical conditions are responsible for the different absorption of the rays. Some general and very definite morphological changes of the protoplasm suggest chemical interpretation very strongly. The conclusions reached were: Different types of carcinoma show characteristically different behavior toward the rays of radium. The behavior depends mainly on the state of differentiation of the different types of carcinoma. The more undifferentiated and embryonic in type the carcinoma is, the more effective is the action of radium rays upon it. On the differentiated types the rays of radium have a hastening effect. If the effect of these rays is proportional to the absorbed amount, the nuclei and protoplasm of different types of carcinoma and benign tissue absorb different amounts of rays.

Lahm [16] propounded the question: Does a microscopic examination make it possible to prognosticate the primary or secondary cure of a carcinoma at least within certain limits? The answer was "Yes," and proven as follows:

"If the sensibility of the carcinoma is 60 per cent of a unit skin dose, then the curative action of the rays extends to a radius of 4.8 cm.; if 80 per cent, to 3.8 cm.; if 100 per cent, to 3.5 cm., and if 120 per cent, to 3.2 cm. If we could determine the radio-sensibility of a carcinoma, we could also determine the radiation dose to cause a primary healing, if we consider

Fig. 1. The equal intensity curves of 50 mg. radium element measured in water.

(1) the bimanual and clinical findings, (2) the radio-sensibility of the carcinoma, and (3) the resorption of the tumor mass, i.e., local healing. The results obtained were that ripe carcinomata require 3000 to 7000 mg. el. hrs.; middle ripe, 4000 to 5000; and unripe, 6000 to 7000; while adenocarcinomata are refractory to any dose."

The changes caused by gamma rays in the carcinomata and revealed by microscopic examination were: (*a*) regular and irregular mitotic nuclei, (*b*) numerous giant-cell formations, (*c*) caryolysis and cytolysis with granulation and vacuolation of the protoplasm, and (*d*) the formation of a zone of reaction around the growth of variable extent composed of plasma cells, lymphocytes, polymorphonuclear neutrophiles and eosinophiles. The eosinophilia

is the best evidence of an early and complete resorption of ripe and middle-ripe carcinomata, while the presence of plasma cells and leucocytes indicates an inability of the host to activate the defensive forces necessary for a degeneration of the carcinoma. The occurrence of eosinophilia runs parallel with the progressive healing of the cancer. Of 156 carcinomata treated between the years 1915 and 1918, 36 had eosinophilia and 120 did not. Of the former, 14, or 40 per cent were cured, 19, or 53 per cent died and 3, or 7 per cent could not be traced. Of the latter, 21, or

FIG. 2. Unripe basal-celled carcinoma of the uterine cervix before radiation treatment.

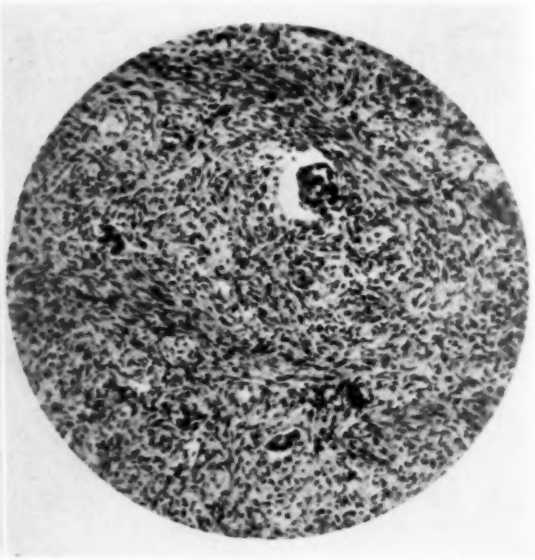

FIG. 3. The histological changes caused within three weeks in the basal-celled cancer seen in Figure 2 with a combined 100 per cent E.S.D. of radium and *x*-rays.

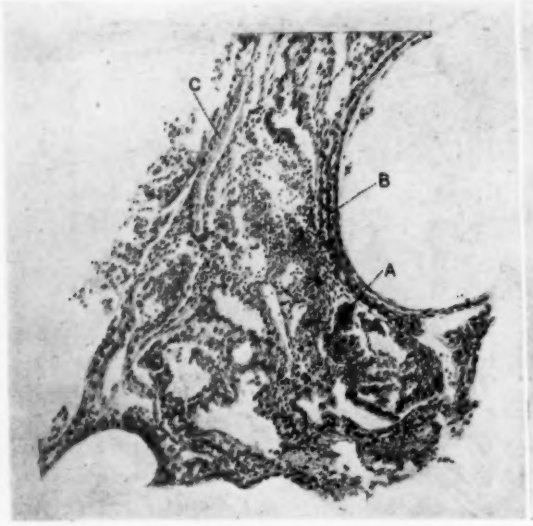

FIG. 4. Adenocarcinoma of the uterine cervix before radiation treatment.

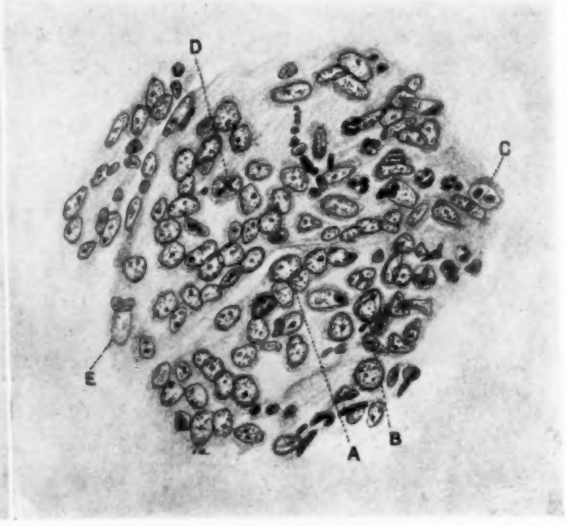

FIG. 5. High-power magnification of an area in Figure 4.

17. 5 per cent were cured, 98, or 81.5 per cent died, and 1, or 0.9 per cent could not be traced.

Lahm states that the virility of the carcinoma cell does not depend on the morphology but on the preservation of the colloidal state of the protoplasm. The protoplasm is injured by the rays, hence dissolution of the reticulum, vacuolation of the protoplasm and finally dissolution of nucleus and cell. During this process poisonous or injurious ions accumulate in the periphery of the carcinoma, stimulating the division of the cells and causing the formation of mitoses and of polymorphonuclear cells.

The investigations of Alter, Lahm and myself permit the deductions that the different types of carcinomata react differently to the action of radium rays and that the different behavior enabled Lahm to express this difference within definite limits in a lethal radiation dose for each type of carcinoma cells.

The action of radium is local. The intensity within tissues or tumors depreciates rapidly. A homogeneous penetration of the entire true pelvis with radium rays inserted intracervical is impossible. If a carcinoma possessed a radio-sensibility of 60 per cent of the full skin dose it could be effectually radiated within a radius of 4.8 cm., according to Lahm. The radius of the true bony pelvis which forms the natural limit of a cervical carcinoma still amenable to radiation treatment is 6 cm. Should the regional lymph-nodes be invaded, they would receive too small a dose. Assuming that Lahm's radium dose is expressed in the per cent of the customary 100 per cent erythema skin dose, the 60 per cent dose is an irritating one and tends to stimulate the growth to more rapid proliferation.

We have investigated the distribution of the intensity of gamma rays of radium.[17] The equal intensity curves are shown in Figure 1. The full skin dose, that is, the 100 per cent erythema skin dose, is attained

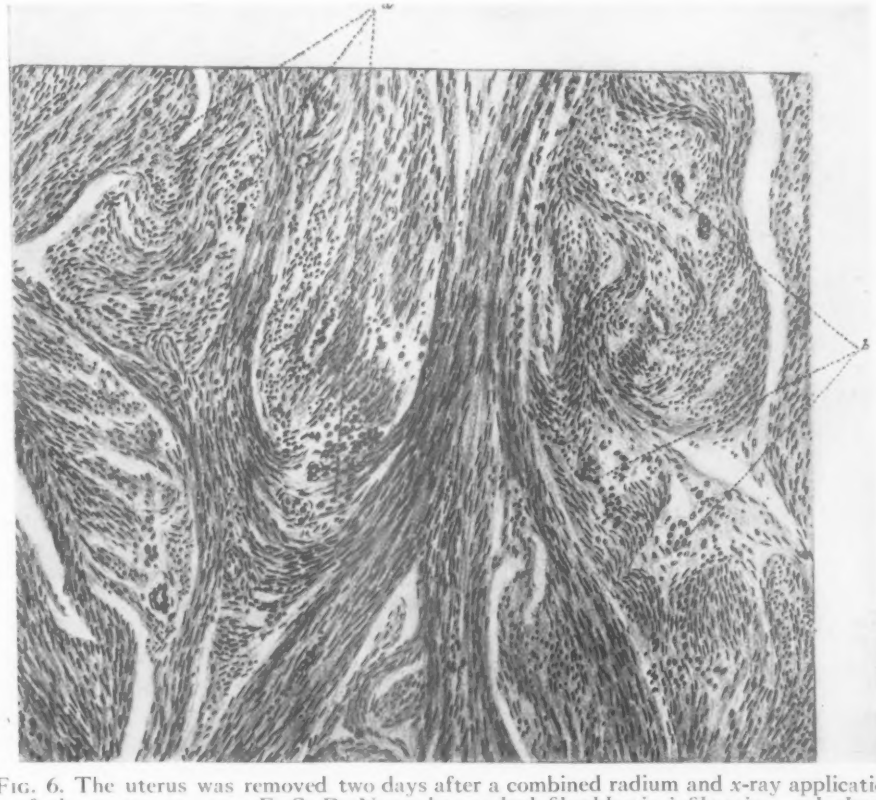

FIG. 6. The uterus was removed two days after a combined radium and *x*-ray application of about 130 per cent E. S. D. Note the marked fibroblastic infiltration and almost complete disappearance of the carcinoma cells.

at isodose 60 with 1600 mg. element hours, (mg. el. hrs.,) at isodose 40, with 2400 mg. el. hrs.; at isodose 30, with 3200 mg. el. hrs.; at isodose 20, with 4800 mg. el. hrs.; at isodose 10, with 9600 mg. el. hrs. The median transverse diameter of isodose 60 is about 3 cm., the longitudinal axis 5.5 cm.; at isodose 40, 4.5 and 6.3 cm. respectively; at isodose 20, 7 and 8 cm.; at isodose 10, apply is with 130 per cent E. S. D. 4200 mg. el. hrs., and with 150 per cent E. S. D. 4800 mg. el. hrs. Assuming that a carcinoma had a radio-sensibility of 100 per cent and occupied an elliptical area of a median transverse diameter of 7 cm. and a longitudinal axis of 8 cm., the carcinoma dose of 4800 mg. el. hrs. would be lethal. Therefore if we use radium alone we can

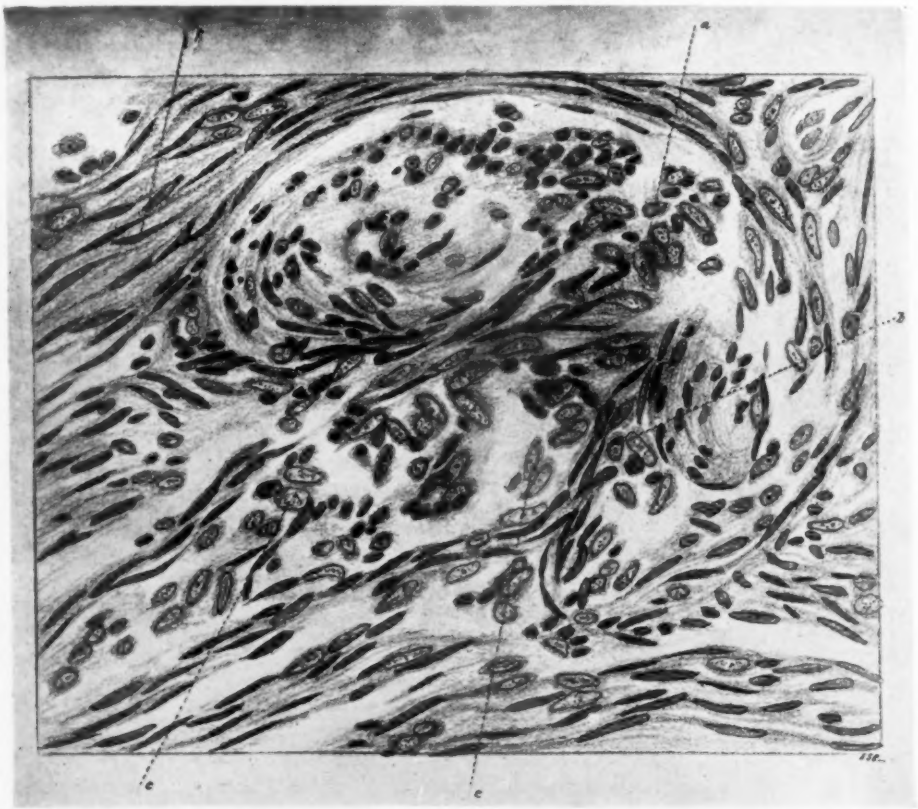

FIG. 7. High-power magnification of an area of Figure 6 to show the degeneration of the nuclei and protoplasm of the cancer cells.

9.5 and 10.7 cm. The object of radiation therapy must be to kill the carcinoma without causing irreparable injury to normal tissues and organs lying within the path of the radiation field. The posterior bladder wall is about 2.5 cm., and the anterior rectal wall about 2.5 to 3 cm. distant from the cervical canal. The permissible maximal radiation dose which the rectal and vesical mucosae will endure without permanent injury is about 130 to 150 per cent of the erythema skin dose. As they lie at about isodose 30 the highest permissible gamma ray dose that we may benefit only a small number of cervical carcinomata. Should the radio-sensibility of the carcinoma be less than 100 per cent and the E. S. D. be 150 to 175 per cent, then the prognosis would be less favorable.

The radiation energy applied must be of the same, or practically the same, intensity at the periphery of the bony pelvic walls as in the center. Such a homogeneity of intensity may be attained either by distributing the radium all through the pelvis or by using a combined application of radium and *x*-rays. Radium may be evenly distributed through the pelvic

cavity by the use of needles containing radium salt or glass capillary tubes filled with radium emanation. Instead of glass capillary tubes, those made of a material soluble in body tissues may be used.[18] These methods necessitate a laparotomy. We have discarded the method of "needling," as the poor results did not warrant a continuation.

The application of a lethal dose to carcinomata causes a destruction of the malignant cells, and to some extent, of normal cells, especially the white blood corpuscles. The split proteins are absorbed and a non-specific protein toxicosis ensues, evidenced by an increase in the nitrogen constituents and a decrease in the chlorides of the blood. This is

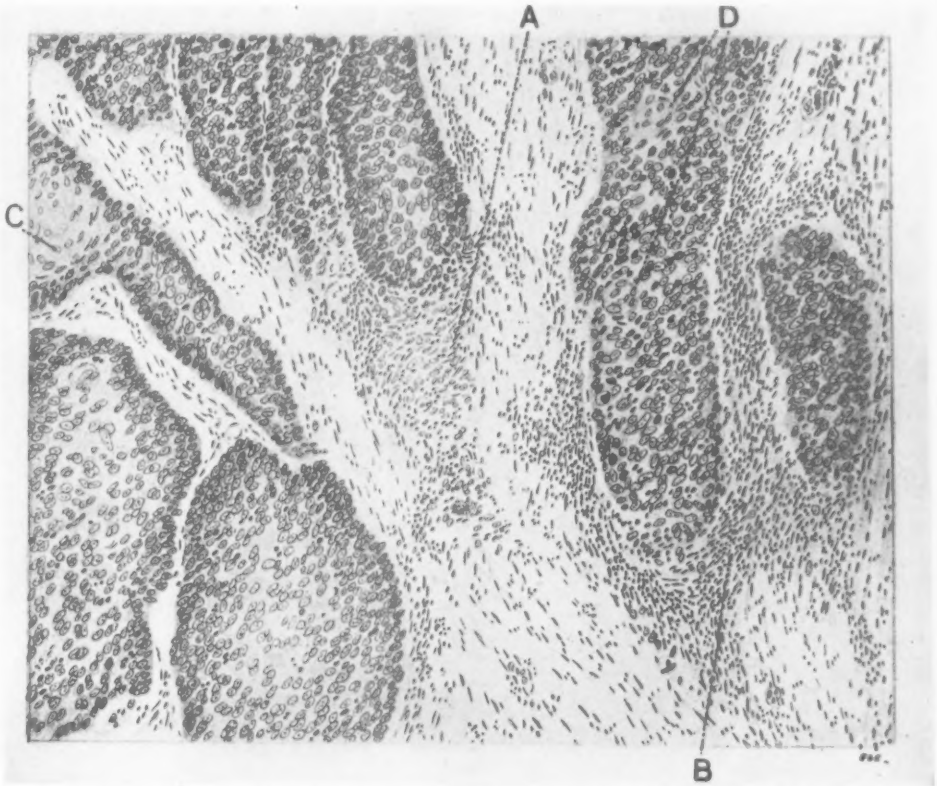

FIG. 8. A squamous epithelial-cell cancer of the uterine cervix before radiation treatment.

The combined application of gamma and *x*-rays enables one to devise a method which assures a homogeneity of radiation intensities all through the pelvis. I shall not discuss this method, but refer to the publications on this subject.[19,20]

These investigations placed us in a position to study the changes produced with measured radiation doses in carcinomata of the uterine cervix. They comprised observations on the relation of the measured radiation energy to (1) the chemical constituents and defensive ferments of the blood, (2) the local palpatory evidences of the disease, and (3) the microscopic examinations of tissues. the more remarkable as Theis and Stone[21] found a low content of non-protein nitrogen and urea nitrogen in the blood of carcinoma patients, while Hirsch and Peterson[22] did not find any changes after radiations. The toxicosis, also, changes the total number of the white blood cells and the percentages of the different white cells. These changes correspond to the typical picture seen in anaphylactic shock. A cancer patient refractory to the rays does not show any disturbance of nitrogen metabolism, the white blood cell count or the percentage of the white cells. The absence of these reactions indicates a negative result from the radiation treat-

ment caused by either a general resistance of the patient (seen especially in advanced cachexia) or an insufficient dose of rays.

The Freund-Kaminer[23] test for carcinomata is based upon the observation that the isolated cells of carcinoma are dissolved by the serum of non-cancerous individuals, whereas this property is wanting in the sera of carcinoma patients.

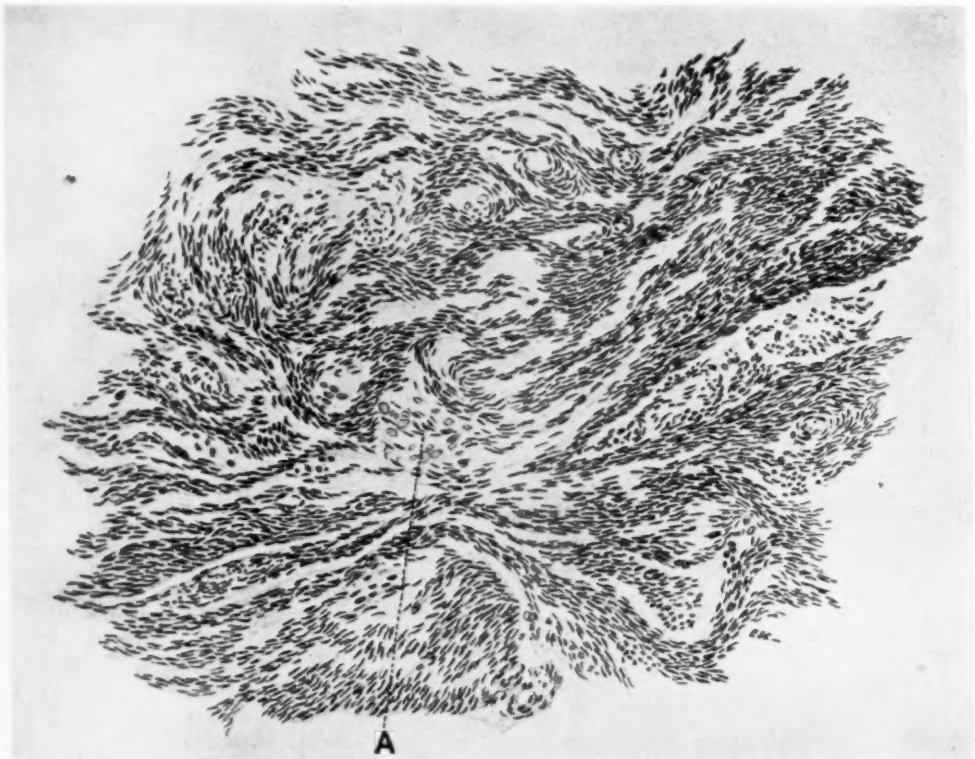

FIG. 9. The uterus was removed three months after the application of about 175 per cent E. S. D. of radium and *x*-rays. Note the connective-tissue formation and the practically fatal absence of malignant cells.

They also showed that if a carcinomatous growth is surgically eradicated, the serum of such patients would reacquire carcinolytic properties. We therefore concluded that if a carcinoma has been completely degenerated by radiations, the blood of such patients should show carcinolytic properties. This assumption was proven to be correct. These investigations will be published in the near future. Whether we shall be able to use the results clinically, or whether they will corroborate the contention that rays can effectually destroy carcinoma, cannot as yet be stated. Herly[24] and Coca[25] studied the diagnostic value of the Freund-Kaminer reaction and they deny it any diagnostic possibilities. However, these conclusions do not interfere with our investigations, as we are testing the relative values in microscopically proven carcinomata.

A lethal carcinoma dose should be followed by negative palpatory findings. The cervix should be healed and the parametria free of any induration. The pelvic organs should become movable and of normal consistency, though scar formation may leave indurated bands behind. The microscopic examination of excised tissue from such a "healed" cervix must reveal total absence of epithelial cancer cells. These two conditions are the criterion upon which we must base the efficacy of the therapeutic value of radiations in cancer therapy. Should local healing continue for five years free of any recurrence, the cure is an anatomic one and complete.

We have kept careful records of the radiation dose applied in 418 consecutive

cases of cervical carcinomata. We preserved the microscopic sections and maintained a thorough follow-up system. The percentage of squamous-cell carcinomata was 60, of unripe basal-cell carcinomata, 15, and of adenocarcinomata, 25. The middle ripe carcinomata are included in the first group, as they show evidence of progressive differentiation and tendency to maturity. They amount to 12 per cent. By means of the isodoses of radium, the absorption graphs of *x*-rays, and the anteroposterior and transverse diameters of the pelvis, we calculated the radiation energy applied.

In 40 cases of squamous-cell carcinomata we had 15 cases of primary healing and absence of carcinoma cells from the tissues, i.e., 37.5 per cent. In the group treated with about 80 per cent E. S. D., the percentage of primary healing was 14.3; in the 100 per cent group, 25 per cent; in the 130 per cent group, 66 per cent; and in the 150 per cent group, 80 per cent. In 10 cases of unripe basal cell carcinomata treated with about 100 per cent E. S. D. we had 5 primary healings, i.e., 50 per cent, and in 16 adenocarcinomata we had 0 per cent healings with 100 per cent, and 66 per cent with 130 per cent E. S. D. The microscopic examinations are reproduced in the accompanying illustrations. Figures 2 and 3 represent an unripe basal-cell carcinoma before and after treatment. Figures 4, 5, 6 and 7 an adenocarinoma; and Figures 8 and 9 a squamous-cell carcinoma treated with 100, 130 and 175 per cent E. S. D. respectively.

We cannot as yet draw any conclusions concerning the future behavior of these primarily healed cases. However, we shall arrange all the cases treated statistically and publish them in a second communication.

We may be permitted to draw the tentative deductions that the lethal carcinoma dose for unripe basal-cell cancers is about 100 per cent E. S. D.; for adenocarcinomata about 130 per cent, and for squamous-cell carcinomata, 150 to 170 per cent E. S. D.

CONCLUSIONS

1. The cell types of cervical carcinomata may be conveniently divided into three groups: The unripe basal-cell, the squamous-cell and the cylindrical-cell adenocarcinoma.

2. The radiation sensibility of these three cell types differs. It is greatest in the immature basal-cell type; less so in the adenocarcinoma and least in the squamous-cell carcinoma.

3. The prognosis of the efficacy of radiation therapy in cervical carcinomata must be based on (*a*) the measured radiation dose; (*b*) the changes occurring in the blood, particularly in the nitrogen constituents and the behavior of the white blood corpuscles; (*c*) a careful clinical examination to determine local healing; (*d*) repeated microscopic examinations made before and after treatment.

4. An attempt has been made to express the lethal carcinoma dose for each cell type of cervical carcinoma in per cent of the full 100 per cent erythema skin dose.

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DISCUSSION[1]

Mr. L. B. Clark, San Francisco, Calif. After listening to these two papers I think there is little left to say and from the standpoint of the physicist I feel that I cannot add anything.

Dr. H. H. Bowing, Rochester, Minn. I have enjoyed these two papers immensely. There is no doubt that our work depends on just such studies. I have always been impressed with the work of Alter. Certainly we can all learn much from his Studies I and II.

Just what is the basis of it all, and what brings about this cellular reaction in the carcinoma cell and body tissue is a complex question. I think we will have to continue in theory until we know more about our biologic and microchemical reactions. Much depends on our knowledge of colloidal chemistry, and it is possible that much of it can be carried out in the laboratory in various ways.

It seems that the radiation reaction as we see it in the tissue, as we know the entity of the radium tube, is comparable to that of penetrating heat. It seems that it would be justifiable to compare the reaction in the heat sense, for we know that the energy of the radium and roentgen tube can be measured in terms of heat units.

As to the sections for study, I have always been very anxious, perhaps too much so, to take tissue for study. I think we should be very careful. Most of these patients are poor risks and the chance of hemorrhage and metastasis through manipulation is very great. If we jeopardize these patients the chance for improvement is very slight, but I think it is justifiable to take sufficient biopsy material for study. If one of my patients is doing well and a section is removed, and at the same time a radium tube placed in close proximity, the next morning the patient's temperature will be 100 to 104° F. We must be very careful on account of the danger of bleeding and infection.

As to the fibrosis, we know that the radium dose that will destroy a carcinoma cell will also induce fibrosis, and an over-production of fibrous tissue must be avoided.

It is encouraging to see some of these inoperable patients return in four to six months apparently cured of their carcinoma. They will respond locally to small repeated doses of radium. It is my custom to place a 50-mgm. tube for a period of fourteen hours, and then repeat at intervals of from two to three days until a 4000 or 9000 total mgm. hour dose is built up. Each interval will help to decide how far to push the treatment. In this manner, many portions of the tumor may be treated, including the deep-lying portions. If we fail, it is probably because the deeper areas of the cervical canal and fundus did not get sufficient treatment. As these patients first present themselves, it is impossible in many cases to place the radium tube deep in the cervical tissue without traumatizing the part, but as time goes on, new portals open up. In my experience the broken dose method is more effective than the intensive single-dose application.

I have never employed needles in primary carcinoma of the cervix. I try to avoid all trauma, using the natural channels for the introduction of the radium tube. As the days go by, these tumors degenerate and new avenues open up, and with care the radium may be placed deeper in the involved area. I am confident that the broken-dose method, administered in from two to four weeks, will always bring satisfactory results.

The eosinophilic infiltration following radium treatment is very interesting. I recall a case of splenomegaly in which splenectomy was performed. About two weeks before the operation

[1] This discussion has reference to the preceding paper by Dr. Withers, as well as to the above.

radium was applied to the splenic enlargement; the tumor was reduced two-thirds in size by the time it was removed. Many sections were studied. The pathologist's comment was that he had never seen so many eosinophiles in any given spleen, and no doubt this was the result of the irradiation.

Concerning the use of a few animals for our laboratory studies, we must be guided by what Wood has shown us: that sarcoma or carcinoma of certain animals may "take" readily in certain months of the year, while in other months the "take" is practically nil. I feel sure that the results should be questioned and the experiments repeated if investigations are carried on with a small group of animals. Such experimentation should be done in laboratories where they have a large amount of material. These variations could easily be attributed to the experimental substance employed, but it would be necessary to rule out the above factor or natural variation before any conclusions could be drawn. It is probable that the chemistry of the patient with carcinoma is comparable to that of the pregnant woman. If pregnancy is considered as a pathologic condition, reaction and many other associated features should be considered, but to me the condition appears physiologic; therefore a plan must be evolved to demonstrate a pure physiologic process.

Dr. D. W. Montogomery, San Francisco, Calif. I did not quite understand the remarks of Dr. Bowing regarding the seasonal variation in the experimental animals.

Dr. Bowing. The work of Wood at the Crocker Institute in New York City is very interesting. Wood can demonstrate with charts showing the number of "takes" in a twelve-month period. There are wide variations; some months the successful inoculations will be very great and in other months they will be very few; this is independent of season and many control factors. It is tedious to explain. A man may be working on 100 animals in a month, injecting, for example, a colloidal material, and may see this reaction or variation. He may conclude: "This is what is doing it; I have found something worth while," but Wood will see these great variations without doing anything to influence the animal. I repeat, therefore, that we must be very careful about accepting the conclusions based on a small number of animal experiments.

In injecting active carcinoma material to bring about "immunity," one must proceed with much trepidation, since animal experimentation demonstrates that immunity does not occur, but instead, wider dissemination and metastasis, and death to the animals.

Dr. W. H. B. Aikins, Toronto, Ont. These highly scientific papers, which show wonderfully good work, will give the men who are using radium a better basis for their clinical endeavors, and we feel much enlightened and encouraged. Their findings are absolutely up-to-date so far as radium therapy is concerned. They both speak with authority. I quite concur with Dr. Withers in his remarks regarding the propaganda in connection with cancer control, that this propaganda is apparently being put forward very largely by those having a strong surgical view, who do not take proper cognizance of the beneficial results obtained by roentgen rays and radium. I hope Dr. Withers' remarks will be given wide publicity.

Dr. Montgomery. We suppose the gamma rays act on the tissue cells in the following way:

In the first place, gamma rays are noxious to all cell life when given in sufficient dosage. The tissue cell consists of a body and a nucleus, and the nucleus is surrounded by a perinuclear case or membrane, which affords it protection. The nucleus is the life center of the cell. In cell division the perinuclear membrane vanishes, and the whole contents are scrambled within the cell. During the time of this cell division the nuclear elements are exposed, and consequently the cell is much more susceptible to the noxious influence of the gamma rays. As the cells in a malignant growth are in more active division than those of normal tissue the gamma rays kill them more readily, and as a rule they are seven times more lesionable than the normal cells.

It follows from the above premises that treating a malignant growth with gamma rays is comparable to sterilizing a culture medium by fractional sterilization. The cells which are in active division today are killed by today's dose of radium, and those of tomorrow by tomorrow's dose, and so on.

Dr. H. J. Ullmann, Santa Barbara, Calif. I would like to add a little something to emphasize what has been said concerning variations in transplants in animals. On Thursday I had the pleasure of visiting Dr. Evans in the department of anatomy at the University of California, to get some rats for similar work. He urged not only that I keep a standard diet, but that the components themselves be standardized. He has found that variation in diet as well as seasonal change may make any work almost valueless. This is speaking of work with rats especially. Anyone interested will find it very profitable to go to Berkeley and see the work of Dr. Evans and talk to him along this line.

Dr. Bowing. Again referring to Dr. Wood's work: he can show you that very seldom does

experimental carcinoma metastasize to the spleen. He explains this phenomenon by the fact that the spleen is a pulsating organ, therefore cells cannot readily lodge to form new growth. The spleen does not produce a substance which will inhibit the growth of the foreign cell. The injection of splenic pulp will not "immunize" an animal any more than the injection of any foreign protein.

Dr. Withers (closing discussion on his paper). My paper attempted to deal briefly with the fundamental principles of radiation therapy from a biologic viewpoint. Much could be said in closing which for the sake of brevity must be omitted. I should like to reiterate a statement made previously that this résumé necessitates making broad statements to which possible exception may be taken, but will in general present the working ideas that we hold in the treatment of neoplastic diseases by gamma and *x*-rays.

Dr. Schmitz (closing discussion on his paper). As far as the removal of the tissue for microscopic examination is concerned, we use a very sharp knife, usually the Parker knife, and make a V-shaped excision from the cervical canal into the vagina. Thus we get a piece of tissue that has the cervical as well as the vaginal mucosa. Of course, there is a great difference of opinion as to whether we should perform a biopsy or not, and I assure you I always do it with a great deal of hesitation. Dr. Ochsner and others are averse to biopsy, stating that they never saw a patient subjected to biopsy who recovered permanently. However, the immediate application of the cautery or radium seals the blood vessels and prevents escape of cancer cells into the blood stream. Microscopic examinations are of the greatest value in the estimation of the efficacy of the radium and roentgen dose.

Dr. Bowing (replying to Dr. Schmitz). My point was that when the patients are first seen, the tumor has so destroyed the anatomy that the cervix cannot be located. The huge mass or ulcerated area will permit the radium tube to be placed in the natural grooves or craters; and then by repeating the treatment once or twice a week the tumor will regress to such an extent that at the end of ten days or two weeks the cervix can be located, and probably the cervical canal can be probed. I have seen the posterior or anterior cervical lips come into view, and then with some assurance that the probe was in the cervical canal, the fundus of the uterus could be palpated, in other words, without traumatizing carcinomatous tissue and yet reaching the deeper portions of the involved area.

Dr. Schmitz (continuing). I believe the cervix to be the best filter for the irradiation that we have, and I insist on the intracervical application of the radium. By placing the patient under nitrous oxid anesthesia there is very little difficulty in exposing the cervix if you use the Sims speculum. You can by careful palpation locate the cervix, and if you know the location of the uterus by bimanual palpation you can place the uterine sounds correctly. Of course, there is always infection present in advanced carcinoma, but these patients have acquired immunity against their own bacteria which they harbor. If infection does occur it is from without. We made consecutive cultures in 250 gynecological cases to study the bacterial flora, particularly in reference to the hemolytic streptococcus. A great many of these patients were operated upon and had a normal convalescence. A few died from septic conditions. The important thing was that none of the patients who had hemolytic streptococci became infected with their own organism, but became infected with an entirely different strain.

I witnessed two post-mortem examinations conducted by Professor Aschoff. In one the radium tube had been pushed into the posterior vaginal fornix and in the other it had gone through anteriorly. Both patients died from a septic peritonitis. The same accident happened twice in our clinic. We placed the patients in bed and watched them carefully, and aside from a slight rise in temperature saw no bad results. I do not wish to say that our methods of sterilization are better than those across the water. Our patients may have had a better resistance, not being undernourished.

We introduced the fractional dose method in 1913, placing the radium capsule for ten or twelve hours every third or fourth day until a certain amount of irradiation had been given. Then we applied the same dose in one sitting, leaving the radium capsule for four days. We did not like the last method. It seemed to prevent individualization in treatment. After that we used seven to eight daily applications, permitting the capsule to remain for ten hours each time. Our present method is as follows:

In order to apply a 100 per cent radiation skin dose to the cervix, three or four fields of *x*-rays are applied. The time duration depends upon the size of the patient. We excise a piece of tissue for diagnosis and insert a 50 mgm. radium element capsule for forty-eight hours. In three or four days we have a complete report on the biopsy, and then we determine the lethal dosage. To a squamous-cell type we give a ninety-six hour treatment and to the basal-cell type a twenty-four hour treatment. We never repeat the treatment. If within six, eight or twelve weeks there is no sign of healing we feel that irradiation will not help the patient.

RESULTS OF DEEP ROENTGEN TREATMENT OF GASTROINTESTINAL MALIGNANCIES*

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THIS paper deals with our experience in treating malignancies of the gastrointestinal tract with deep radiation for a period of over a year, and is limited to 60 cases. We have elected to present our observations on this phase of our deep therapy work for two reasons:

1. Because the literature is barren of all reference to results obtained by the deep radiation of malignant neoplasms of the esophagus, stomach and intestines, and because there is no available information as to technique, indications, complications, etc., aside from a few brief reports on treatment with radium.

2. Because, contrary to the opinion generally held, satisfactory results were obtained in a fair percentage of cases, not only in controlling many of the unpleasant symptoms, but actually in controlling the extension of the disease itself, and in some cases, the eradication of the disease.

REVIEW OF CASES TREATED

Our series includes 6 cases of cancer of the esophagus; 25 cases of cancer of the stomach; 4 of the cecum; 3 of the sigmoid and 17 cases of cancer of the rectum. We have included in this report 1 case of a primary cancer of the liver, 1 case of late secondary cancer of the liver, with primary in the breast; and 3 unclassified tumors of the upper abdomen which deformed the stomach and resulted in delayed gastric evacuation.

The diagnosis in every case was made on clinical and roentgenological evidence, and in many cases, on operative and microscopical findings. Furthermore, the stomach cases were as a rule classified as inoperable, and several of the rectal cases had already undergone resection, and the cases were referred for treatment of secondaries.

1. *Lesions of the Esophagus.* A review of the results in our cases of lesions of the esophagus shows that of the 6 treated, only 1 is alive. However, in all the cases, studies of deglutition following treatment demonstrated a definite reduction in the extent of the lesion and a resulting improvement in function of the esophagus.

In analyzing the causes of death in the fatal cases, it is recorded that 2 of the cases died from pneumonia as a result of esophageal-bronchial fistula, 2 died apparently from cachexia, and a 5th died suddenly from a cardiac complication. In all these cases the lesion was localized in the middle or lower third of the esophagus; i.e., in a place hardly accessible for the radiation; and only in the 6th case, which is still alive, was the lesion confined to the upper third. This case first came for treatment eight months ago, with enlarged cervical glands, which had a typical carcinomatous appearance, but the primary lesion, although suspected in the upper portion of the esophagus, could not at that time be demonstrated. The enlarged cervical glands only were treated, and they disappeared promptly after the treatment. Two months later, the patient returned for examination, complaining of difficulty in swallowing. Examination at this time revealed the presence of a typical carcinomatous lesion in the upper third of the esophagus (Fig. 1). This lesion was treated by deep radiation and two months later a disappearance of the lesion could be demonstrated (Fig. 2).

In 4 of the cases treated we used roentgen rays entirely; in 2 cases we applied radium locally in addition. We think the latter method should be preferred whenever possible. Also postradiative dilatation of the esophagus is advisable for a number of weeks following the treatment.

2. *Lesions of the Stomach.* Of the 25 cases presenting gastric lesions, 14 are

* Read at the Fourth Annual Meeting of the Central Section of THE AMERICAN ROENTGEN RAY SOCIETY, Louisville, Ky., Feb. 24, 1923.

dead and 1 shows no improvement. Of the remaining, a number are clinically well and others show improvement of varying degrees. In 2 of the cases showing marked defects at the original examination, plate studies failed to reveal any evidence of an infiltration of the gastric wall later. Figures 3 and 4, and Figures 5 and 6 show these cases.

In another case, deep *x*-ray treatment was combined with surgery. The tumor being on the pylorus (Fig. 7) a resection of the pylorus was done, together with posterior gastrojejunostomy, but the microscopic examination of this specimen has shown that the lesion, which was a cylindrical-celled carcinoma, has extended beyond the margin of the excision. Therefore, deep *x*-ray therapy was given, following the operation, and the patient has been well for more than a year (Fig. 8).

Of those who died, 3 died within ten days following the treatment. Of the rest, it is reported that they were relieved of pain, vomiting, and hemorrhages for a period of two to six months. In 3 of the cases in which ascites occurred shortly following repeated aspirations, there was a clearing up of the abdominal fluid, without further recurrence. (In this connection we have observed that in 3 other cases showing ascites, with the primary lesion distinct from the gastrointestinal tract, the fluid disappeared following the treatment over the abdomen.)

FIG. 1. Carcinoma of the upper third of the esophagus. Partial obstruction of the esophagus by the tumor mass at the level of the sternoclavicular region, the barium mixture remaining in the part of the esophagus above the lesion for five or ten minutes. Beginning dilatation of the upper portion of the esophagus. Considerable enlargement of the cervical glands on the right side.

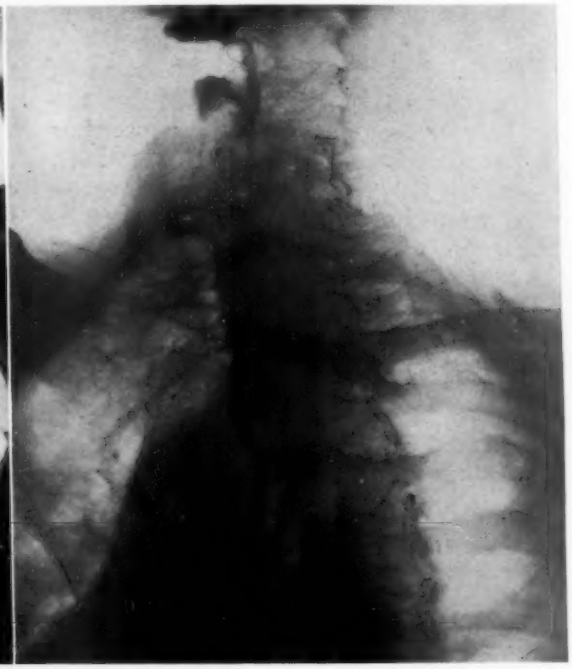

FIG. 2. Same lesion, two months after deep *x*-ray treatment. Normal lumen of the esophagus at the site of the lesion. No obstruction and no retardation of the barium mixture above the lesion. No difficulty in swallowing. The enlargement of the cervical glands has disappeared. This plate was made by flash exposure while patient was swallowing the barium mixture.

3. *Lesions of the Intestinal Tract.* In all 4 cases of cancer of the cecum, the results were gratifying, 3 of them being alive after one year, and the condition of the patients showing improvement over that at the time of the original treatment. Of the 3 cases of involvement of the splenic flexure and sigmoid, the patients are alive, and their condition shows clinical improvement.

4. *Lesions of the Rectum.* Of the rectal cases, 9 patients are dead, and the remaining 8 show either improvement or a com-

plete control of the signs and symptoms (Figs. 9 and 10) with one exception, where a rectovaginal fistula developed as a result of the treatment. This case gave a history of tumor of the breast of a carcinomatous nature. After two years there was evidence of a cancer of the uterus, and later a cancer of the lower bowel. The patient had had radium treatment, superficial *x*-ray treatments, and four months ago a resection of 8 in. of the lower large bowel. About four weeks ago, inoperable and instead, a specimen was taken for microscopic examination. This showed multiple primary carcinoma of the liver, springing from multiple adenoma of the bile ducts. Immediately after the deep *x*-ray treatment all the symptoms subsided; patient gained 30 lbs., and has been well ever since. Repeated functional tests of the liver were made and these showed normal. The patient has been back at work now, for a period of over a year.

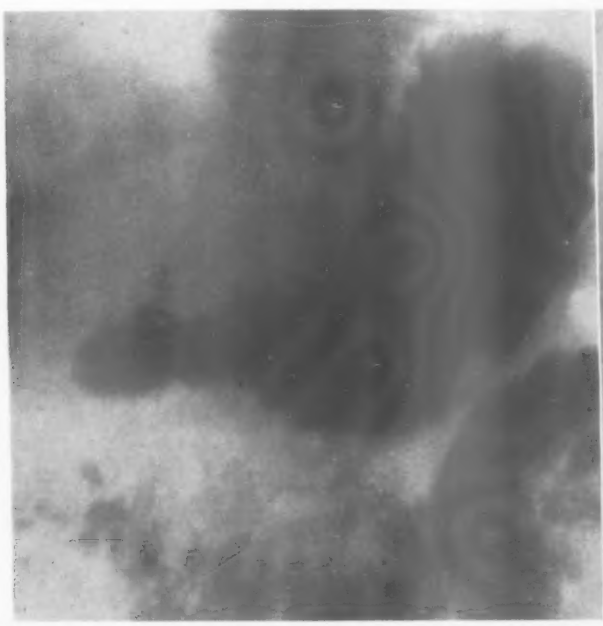

FIG. 3. Carcinoma of the lesser curvature of the stomach. Constant defect in the middle third of the lesser curvature, with irregular outlines. Atonic stomach. Patient rapidly losing weight.

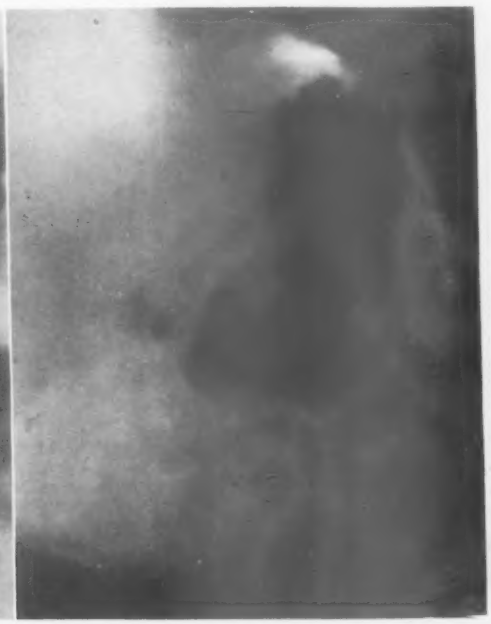

FIG. 4. Same eight months after deep *x*-ray treatment. Defect has disappeared. Three-wave peristalsis; normal appearance of the stomach. Patient gained 36 lbs. and is without any symptoms.

there was a rapid recurrence of the pelvic tumor, a large mass being discovered between the colon and the uterus. Three weeks following a full carcinomatous dose, this mass broke down and discharged through the vagina. The patient now has a fistulous tract connecting the sigmoid and vagina.

5. *Lesions of the Liver.* We have treated the liver by deep roentgen rays in 1 case of primary carcinoma and in several cases of secondary metastases. The case of primary carcinoma of the liver was in a young woman, thirty-two years of age. The patient was examined by incision one and one-half years ago, but found

While secondary metastases of the liver were treated successfully in a number of cases, however, the final prognosis in these cases is not good. In one of our cases, operation was performed eight months ago for carcinoma of the sigmoid. At the operation a large tumor mass of the sigmoid was found with extensive metastases to the liver. Consequently, the patient was declared inoperable and only a colostomy was made. Following a heroic radiation of the whole abdomen and the liver, the patient's condition improved so much that six months later removal of the remaining carcinoma of the sigmoid was made, and the patient

is now without any symptoms. In another case, where we treated the liver for metastases, the primary lesion was in the breast. Radical operation of the breast was performed two years ago, without local recurrence. But, two years later, metastases developed in the liver and abdomen with accompanying ascites. Following deep radiation, the liver is reduced to almost normal size, the ascites has disappeared and the patient's condition is greatly improved (Figs. 11 and 12).

FIG. 5. Carcinoma of the lesser curvature of the stomach. Large filling defect extending along the greatest part of the lesser curvature. Indefinite contour of the pylorus. Viewed laterally, the stomach shows irregularity of the anterior wall. There is no evidence of peristalsis. Patient rapidly losing weight.

FIG. 6. Same nine months after deep *x*-ray treatment. Normal outline of the stomach. Two-wave peristalsis. Patient gained 20 lbs. and is without any symptoms. (Note. This patient has recently developed lung and pleural metastases, and died as a result, one year after the deep *x*-ray treatment was given. The stomach remained normal.)

6. *Unclassified Lesions.* In the unclassified cases, one was apparently a tumor of the pancreas with involvement of the biliary tract, with resulting jaundice. At the time of beginning the treatment, the patient could retain no food, and was completely prostrated; but after the reaction from the treatment, there was a rapid return to health. The patient remained well for eight months, when there was a return of the jaundice. Following a second series, the symptoms again cleared. In a second unclassified case there was a large upper right quadrant mass which deformed the stomach (Fig. 13) but was apparently not of the stomach; there was a twenty-four hour residue and the patient was reduced to 75 lbs. Following the treatment there was a gradual improvement in her symptoms, and at this date she weighs 40 lbs. more than at the time of beginning the treatment, and has no untoward symptoms. The plate at this time shows no pressure defect on the stomach, and there is a good rate of gastric evacuation (Fig. 14).

A third unclassified case was a deforming lesion of the stomach and duodenum, probably from a retroperitoneal lymphosarcomatous gland. The patient had lost 100 lbs. in weight and presented symptoms suggesting pressure on the pancreatic duct. Twenty-four hours following the first dose, there was a reduction in the size of the tumor, and in four days no defect of the stomach was demonstrated.

TECHNIQUE

1. *Localization of the Lesion.* It is extremely important that the exact localization and extension of the lesion be made before deep therapy is undertaken, and all diagnostic means should be used in order to determine this. Preliminary gastrointestinal examination by means of the barium meal was used as a routine measure, and wherever possible, an exploratory was done, and if the case was at all operable the surgical indications were carried out. In these cases combining surgery, the tumor was localized with the aid of the surgeon, and the extent of the lesion was projected on the skin surface.

2. *Preparation of the Patient.* The gastrointestinal tract should be empty during the exposure of the patient to radiation. If previously a barium meal was given for examination, this should be removed by purgatives or enemata, so as to prevent unnecessary secondary radiation of the bowel mucosa from the barium.

We find it advisable to put the patient on a fat and acid-free diet, and to prescribe alkalies during the treatment, so as to combat the acidosis. In cases with the nervous symptoms predominating, morphine or other sedatives may be administered, but as a rule this medication increases the nausea. Therefore we prefer to avoid the administration of such drugs, whenever possible.

A preliminary blood examination should be made in every case. A low red cell count or a low hemoglobin index does not contraindicate treatment, for in cases of cancer of the stomach hemorrhage is a common symptom, and there is a tendency for the deep therapy to control these hemorrhages. In one case with a far-advanced carcinoma of the stomach the blood count by repeated examinations showed only 300,000 red blood-cells. Imme-

FIG. 7. Carcinoma of the pyloric end of the stomach (microscopically, cylindrical-celled). Five-hour plate, showing about 80 per cent gastric residue and the presence of an annular lesion at the pylorus. Patient rapidly losing weight.

FIG. 8. Same, one year after deep *x*-ray treatment, combined with resection of the pyloric end of the stomach. No evidence of any malignant infiltration. Stomach functioning well. Patient gained 25 lbs. and is without symptoms.

FIG. 9. Carcinoma of the rectum. Definite filling defect in the lower portion of the rectum, due to obstruction by the tumor.

FIG. 10. Same, five months after deep *x*-ray treatment combined with radium. Lesion almost entirely disappeared. Good filling of the rectum. Patient symptomless.

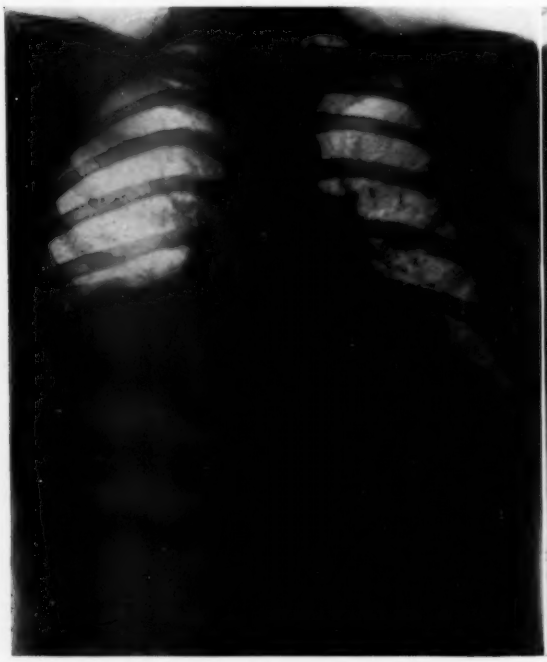

FIG. 11. Metastatic carcinoma of liver, omentum and lower part of right lung after carcinoma of breast removed two years ago. The right diaphragm leaf is considerably pushed up as a result of the liver enlargement. Two metastatic noduli visible in the lower part of the right lung field. The lower border of the liver reached as far as the right iliac crest. Ascites; marked cachexia.

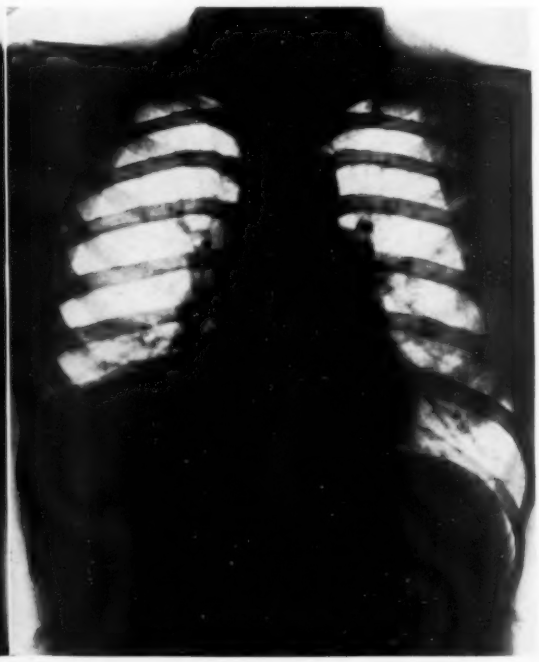

FIG. 12. Same, three months after deep *x*-ray therapy. There is normal height of the right diaphragmatic leaf. Metastatic noduli in the lower part of the right lung disappeared. Lower border of the liver almost normal. Ascites disappeared. Patient gained about 20 lbs. Condition very much improved.

diately following the treatment there was a gradual improvement in the blood condition and this improvement was maintained. The patient lived three months after the treatment, and all of his symptoms during that time were under control. In this case the red blood count increased to 800,000 within a week of the treatment, and this, we believe, was due both to control of the hemorrhage and the possible stimulation of the spleen from the scattered radiation.

40 to 60 cm. The effective wave-length of the rays produced under these conditions is $\lambda_{eff.} = 0.137$ A.U. (using Duane's table) and at a 50-cm. skin target distance, the depth dose (10 cm. below the skin) = 45 per cent. We found that the determination of the distribution of the intensity of the rays at different depths of the tissues is a very important factor and therefore it should be determined individually for every installation under all conditions to be used; such as when changing filters,

FIG. 13. Malignancy of the upper right quadrant; exact type not determined. Because of the far-advanced age, no laparotomy was possible. There is marked pressure defect of the lesser curvature of the stomach, with 80 per cent gastric residue at five hours', and about 30 per cent residue at twenty-four hours' examination. A large tumor mass, the size of a pineapple, is palpable in the right upper quadrant. Patient's condition is rapidly deteriorating.

FIG. 14. Same, nine months after deep x-ray treatment. Pressure defect of the stomach has disappeared. Normal appearance of the stomach with normal rate of evacuation. No tumor mass is palpable in the abdomen. Patient gained 40 lbs. and is without any symptoms.

3. *Dosage.* In all gastrointestinal carcinomata, we project as much as 110 to 130 per cent of the skin erythema dose over the lesion, and over the secondaries, if present. This, of course, has to be given through several portals of entry, using the cross-fire method. We have confined our treatment to the following factors: 200,000 volts (peak), with 1.3 mm. Cu. and 1 mm. Al. filters, large portals of entry (20 × 20 cm.) the skin target distance varying from

size of fields, skin target distance etc. We found that by using the different so-called "intensity charts" now on the market, without control-measurements and adaptation to one's own installation, grave errors may be committed; and this, of course, greatly influences the results to be obtained. At the beginning, we used the Dessauer-Vierheller charts, which are the most commonly used, but soon we found that the figures on these charts are too

high for American transformers, and that the patients treated, using the calculations of these charts, are far under-dosed. For the conditions mentioned above, for example, the Dessauer-Vierheller charts indicate a depth dose of 56 per cent, which for a lesion lying 10 cm. below the skin and cross-fired through three portals of entry makes a total difference of over 30 per cent. Such an underdosage of the lesion would not produce the biological reaction desired, and in consequence the results would not be the ones expected. Dr. Glasser explains in detail the reason of these differences in the measurements, and he arrived at the conclusion that it is mainly due to the measuring of the coefficient of weakening μ_{water} which is used in the Dessauer-Vierheller charts for the characterization of the quality of the rays. It is certain that by using Dessauer or any other intensity charts for measuring the dosage to be administered, an adaptation of these charts to one's own installation is more than necessary.

With regard to the administration of the dose, we think it should be given in as short a time as possible; but in cases where marked anemia is present as a result of severe cachexia, the treatment should be prolonged and time should be given the patient between the treatments to absorb part of the destroyed tissues.

4. *Repetition of Treatments.* Our experience is that such a massive dose given in one single series cannot be considered as a "killing dose" and a repetition of the treatment is necessary. Usually the reaction following the projection of such a dose is so severe that it persists for several weeks. Therefore, it is only rarely possible to repeat the treatment earlier than two months after the first treatment. Eight to twelve weeks is the usual time before the patient returns to normal condition. A careful examination of the blood and of the bowel function is necessary before a repetition of the treatment is decided upon. If the blood pictures have not yet returned to normal, that is, to the state where they were before the first treatment was given, or if the patient still shows signs of disturbed bowel function, under no condition should the treatment be repeated. In 2 of our cases, because of the very rapid spreading of the cancer lesion, we disregarded these rules and both patients died ten days following the second exposure. We could not determine in these 2 cases the exact cause of death, but we concluded that it was due to too early application of the second dose.

5. *Damage of Normal Tissues during the Exposure.* In treating malignancies of the different parts of the gastrointestinal tract, we expose, of course, normal tissues; and due regard must be paid to these structures.

(*a*) When treating lesions of the esophagus, the exposure of the *lungs* should be avoided as much as possible. The lesion should be cross-fired through the different portals of entry in such a way that very little of the lung fields should be exposed. It is now generally recognized that heavy radiation of the lungs produces fibrosis of these organs, which in cases of exposure of both sides may be fatal to the patient.

(*b*) In the treatment of lesions of the stomach, or of the upper quadrants of the abdomen, especial attention should be given to the *suprarenal glands*, for over-radiation of these organs may produce death in comparatively few days. It has been determined that 70 per cent of the skin erythema dose over both suprarenals is usually fatal. In one of our cases, following three exposures of the upper abdomen, such a severe suprarenal disturbance appeared that we had to interrupt the treatment. The blood-pressure increased from 120 to 260 in three hours and the patient manifested severe toxic symptoms. However, no permanent damage was done in this case because the patient has fully recovered and has remained well after four months. While it is not always possible to protect absolutely both of the suprarenals, it is of the greatest importance that one be left outside of the field of radiation. In order to determine the exact situation of these organs, we usually locate, radiographically, the position of the kidneys and then draw conclusions as to the relation of the suprarenal bodies. In none of our

cases of carcinoma of the stomach did we detect symptoms that could be explained by suprarenal disturbance.

(*c*) Due regard must be had for the *mucous membrane of the intestines*, when treating lesion of the intestinal tract. 140 per cent of the skin erythema dose is considered as the lowest limit supported by the mucosa of the large intestines without serious destruction. If diarrhea appeared ten days after the treatment and lasted for two or three days, this is a sign that a proper dose was given over the lesion. Where the dose exceeds 140 per cent of the erythema dose, serious damage will be done to the intestinal mucosa. If there is evidence of such serious injury to the mucosa at the time of the first series the dose given at the second series must be definitely limited.

(*d*) In none of our cases have we had any permanent damage done to the *skin*. In some hypersensitive patients we get erythema of the second degree, but this is easily and satisfactorily controlled by Dodds' mixture. By using proper technique, the possibility of skin damage is so minimized that this question can be entirely disregarded.

6. *Postradiative Treatment.* In treating malignancies of the esophagus there is a profound reaction manifested by dysphagia and spasm with intensive pain on swallowing. Anodynes should be administered in these cases and regular two-hour feedings by soft diet should be introduced.

After the treatment of carcinoma of the stomach or of the intestinal tract, there is usually a very severe nausea and vomiting for two or three days following the treatment. To control these symptoms it is necessary for the patient to lie absolutely quiet in a well-ventilated room, and alkalies (bicarbonate of soda, tribasic citrocarbonate, etc.) should be administered in order to combat the acidosis. The application of ice bags over the abdomen will also greatly relieve the symptoms. The administration of cerium oxalate in combination with essence of pepsin often relieves nausea. In very far-advanced cases, hypodermoclysis should be done every two or three days, in order to facilitate elimination of the toxins. Also rectal feedings should be given. The symptoms of the reaction following the treatment usually last from three to four weeks, and only then does the condition of the patient start the return to normal.

CONCLUSIONS

1. Deep *x*-ray therapy, in combination with surgery, or alone, is indicated in all malignancies of the gastrointestinal tract.

2. Palliative results are obtained in a large number of cases, in controlling many unpleasant symptoms and checking temporarily even the extension of the disease itself.

3. Eradication of the disease may be expected in early cases, especially when combined with surgery. Considering the short period of observation (one year) no statement can be made as regarding recurrences.

4. A careful measurement of the dose to be given is necessary. One single massive dose of deep *x*-ray cannot be considered as a "killing dose." Treatment should be repeated in six to twelve weeks.

5. Exact localization of the lesion, preparation of the patient, and careful postradiative treatment are very important parts of a successful deep *x*-ray treatment of the gastrointestinal lesions.

6. Normal tissues should be protected. Special attention should be given to the lungs, suprarenal bodies and the bowel mucosa. The skin damage is minimized to almost nothing.

TREATMENT OF A CASE OF PRIMARY MEDIASTINAL TUMOR OF THE LUNG BY X-RAYS AFTER MEDICAL RESOURCES WERE EXHAUSTED*

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THE importance of making a thorough physical, chemical and *x*-ray examination of every doubtful case is being more and more emphasized by the medical profession and demanded by the laity of the present day.

The *x*-ray man has his difficulties in differentiating positively certain pathological lesions. He cannot be too certain of any lesion without the proper presentation of the clinical side of the case and a thorough knowledge of the differentiation of similar shadows. It is interesting to observe how rapidly certain pathological lesions of the lungs are being differentiated and classified, but we shall always have certain exceptions to the general rules, and many conditions are complicated.

I wish to add another to the many already reported cases of intrathoracic shadow arising from the mediastinum; presumably a primary mediastinal tumor. From the roentgenogram of the chest presented, one might consider the area of increased density due to a caseating brachiobronchial gland, aneurysm or a benign or malignant growth. To the patient, the correct and early diagnosis is most important before the area could grow larger, or, if malignant, before there is danger of metastasis.

This case is interesting because of its history and the apparent successful results of *x*-ray therapy after other medical procedures failed.

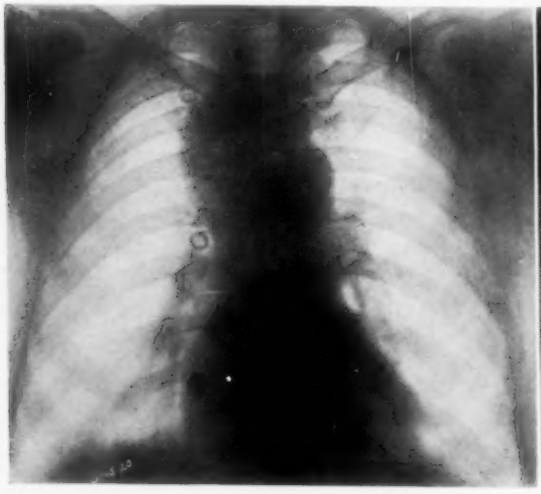

FIG. 1. Made May 15, 1920. Shows a definite, smooth, elliptical shadow just opposite the arch of the aorta. Diameter of the large blood-vessels and tumor measures 9 cm.

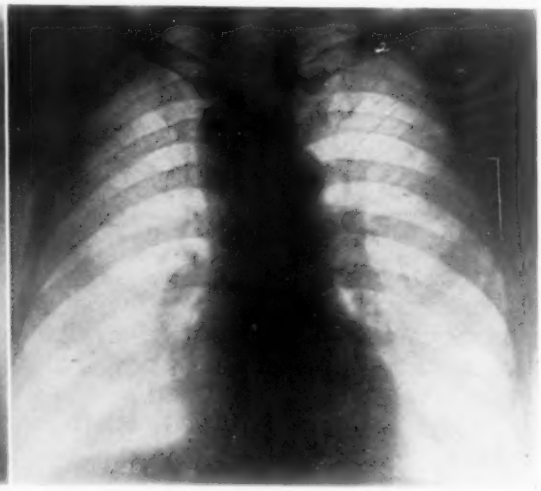

FIG. 2. Made July 17, 1920. Shows the area of increased density decreasing in size in all directions. Large blood-vessels and tumor measuring 7.3 cm.

CASE REPORT

Male, American, fifty-two years old, employed as a section-hand on the railroad, height 5 ft., 9 in., weighing 138 lbs. on May 15, 1920. His family history is negative. He has a marked cachectic appearance and sallow complexion with a history of progressive increasing weakness and loss of weight (lost 6 lbs. during the previous month). He is very nervous from constant

* Paper submitted with application for membership in THE AMERICAN ROENTGEN RAY SOCIETY, 1922.

coughing, shortness of breath and pressure effects.

This cough, he states, started twelve years ago in the springtime. At first this irritation would subside in the summer season and then return in the fall and winter. He has had the persistent, irritating cough all the time for the last four or five years. The sputum is negative as to tuberculosis, and there has been no discolored sputum at any time, nor could I solicit the record of his having had a temperature at any time, nor any palpable glands in the neck or other location.

FIG. 3. Made September 21, 1920. Tumor shadow has practically disappeared.

The patient was thoroughly examined, with the following report:

"With the patient on the left side one can hear, in the third interspace in the third mid-clavicular region, when he has blown out his breath and held it, a loud systolic murmur in this area. The question was raised at once of the possibility of there being an aneurysm, based on a luetic aortic infection."

He had been treated for lues several years ago with a course of "606." At present he has a negative Wassermann test. Mercury was given without improvement.

The patient said he had typhoid fever in the fall of 1919.

On making a fluoroscopic and plate examination at this time I found the following: A rounded mass extending upward and outward from just above the arch of the aorta on the right. I was unable to get definite pulsation, corresponding to the pulsation of the arch. In the plates taken an elliptical mass is seen on the right; it extends from the inner border of the fourth rib posteriorly down to the seventh interspace posteriorly. It is more in front, and extends out about 2 in. from the median line; its border is perfectly smooth, while that with the aorta shows a pulsation and is somewhat hazy.

Doubtless this is a new growth rather than an aneurysm. The trachea is not displaced and comes down in the median line between this and the aorta; the lungs are otherwise normal.

A roentgenogram of the heart taken 7 ft. from the target shows its shadow within normal limits. The apex is under the sixth rib, 8.2 cm. to the left of the median line. Long diameter of the heart 14.8 cm. Transverse diameter 13.6 cm. Diameter of the great blood-vessels 6 cm. Diameter of the great blood-vessels and tumor shadow 9 cm. Diameter of the chest 28.5 cm.

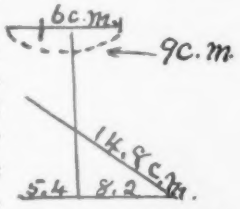

FIG. 4. Shows the diagram of the heart measurements taken from a target distance of 7 ft.

Treatment. After the first deep *x*-ray treatment the irritating cough began to lessen, and the patient improved steadily both in weight and strength, treatments being given directly over the mediastinum and occasionally over the right supraclavicular region, also through the back toward the mediastinum.

Roentgenograms of the heart were taken 7 ft. from the target, two months apart for a time, showing gradual disappearance of the mediastinal tumor.

Treatments were given at intervals of three weeks from May 15, 1920 to August, 1920, using 8½ in. spark-gap with 4 mm. Al. and a thickness of sole leather for filters, and using a 10 in. anode distance, and 25-30 ma. min. The patient gained in weight from 138 to 160 lbs. The treatment was lengthened to once a month for three months, after which he was given a rest of three months. In February, 1921, the patient called my attention to two palpa-

ble infected lymph-nodes the size of English walnuts in the left supraclavicular region, which area I had not treated previously. I was hoping one of these glands might be removed for diagnostic purposes; but the patient objected, and after two treatments by the *x*-ray alone one month apart, these disappeared.

The patient reported in September, 1921, when I could see no evidence of the malady, and again on April 28, 1922. He tells me he weighed 206 lbs. in January, 1922, when his physician advised him to restrict his diet.

NOTE. September 29, 1923. I have seen this patient lately. The tumor has not returned, and while he is working every day, he is rather weak.

It is interesting to note how long this man showed definite signs of pressure symptoms (twelve years) and how slowly the mediastinal shadow increased in size. The appearance of this area of increased density does not show the infiltrative appearance of a carcinoma, but a definite, smooth enlargement. His extreme asthenic condition gradually lessened after *x*-ray treatments were given. He now has the appearance of a perfectly healthy man with a normal endurance.

RESULTS WITH MODERN RADIOTHERAPY IN BLADDER TUMORS*

BY CHARLES GOOSMANN, M.D.

CINCINNATI, OHIO

IN checking up the results of the first year of high voltage roentgen treatment of bladder tumors, the 15 cases under treatment in that period (ending November, 1922) showed six failures and nine successful results. All cases in which the tumor was no longer visible on cystoscopic examination were counted successful, though some of these may show future recurrence. None of the tumors were submitted to microscopic examination. As Cabot says:[1] "There has been an interesting change of opinion regarding the relative frequency of benign and malignant papillomata. . . . The trend of opinion, today, is unquestionably to consider as malignant the majority of papillomata, and that ultimately all papillomata tend to become malignant." And Keyes writes:[2] "Papilloma of the bladder is often a malignant growth, even when the microscope reveals no malignancy about it." All our cases were, therefore, considered at least potentially malignant.

RESULTS

The 15 patients are divided into three groups, according to the treatment:

Group I includes 3 cases, all failures. All of these had roentgen treatment, but no radium, before coming to me.

Group II consists of 3 cases, with one success. Each of these had a preliminary suprapubic cystotomy. The successful case had the tumors cauterized through the bladder opening. Of the two failures one had radium tubes inserted in the bladder and the other had radium needles embedded in the tumor at the trigone.

Group three contains 9 cases with one failure. All of these had what I would call the preferred treatment—high voltage roentgen rays, combined with radium, as described under technique. Three of the 8 successful cases in this group had fulguration treatment after radiotherapy. One of them undoubtedly needed the fulguration, as the tumors were not gone after two courses of radiotherapy. The other 2 had only one course of radiotherapy; and in one of them, at least, the improvement was so marked that the tumor would probably have disappeared completely after another similar treatment.[1]

One of the successful cases of this group

[1] This patient has had a recurrence in spite of numerous fulguration treatments; and received a second course of radiotherapy in May, 1922.

[1] CABOT, H. Modern Urology. Philadelphia, 1918, ii, 198.
[2] KEYES, E. L. Urology. New York, 1917, p. 495.

* Read at the Fourth Annual Meeting of the Central Section of THE AMERICAN ROENTGEN RAY SOCIETY, Louisville, Ky., Feb. 24, 1923.

was still bleeding six weeks after treatment. The tumor was only slightly smaller. As the patient was unusually large, she was given another series, consisting of two hours' anterior and ninety minutes' posterior treatment. This caused severe reaction on the abdomen, but the bladder symptoms cleared up and the cystoscopic report was still good ten months after the last treatment.

TECHNIQUE

Simpson,[1] in discussing the treatment of cancer of the bladder, says: "It is worse than useless to apply radium blindly by means of an ordinary rubber catheter to the interior of the bladder." He advises direct application to the tumor through the urethra or a suprapubic opening. He does not use the roentgen rays.

Cabot,[2] believes: "It is now definitely settled that the endovesical method (fulguration or radium) is the treatment of choice for all papillomata, single or multiple, benign or malignant, and that suprapubic attack is only justifiable in exceptional cases."

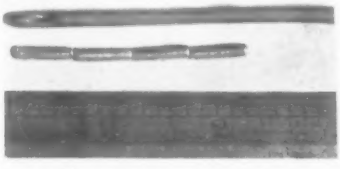

FIG. 1. Four radium tubes and catheter for insertion into the bladder.

I feel that bladder tumors are best treated by a method that reaches every spot of the bladder and the surrounding pelvis, with the largest radiation dose that can safely be administered. This requires the use of radium and roentgen rays in combination. The radium applicator for the bladder consists of four steel tubes containing a total of 51.3 mg. radium element. These tubes are each 12.5 mm. long and have a wall thickness of 1 mm. The four tubes are inserted, without further filtration, in a soft rubber catheter, No. 12 or 14 French. The catheter must be very elastic—I use the Eynard brand (model of Dr. Wishard).

This is inserted into the bladder and left in for six or eight hours, which may require several insertions. I have given twelve hours in one case without damage. The patient is instructed to turn on his sides, back and abdomen at hourly intervals, to distribute the action. The use of four tubes gives a long source of radiation, so the distant effect is improved, as compared with a point source of radiation, where the law of inverse squares applies.

For cross-fire nine standard steel radium needles of 10 mg. each are used in three brass screens, which are placed tandem in a rubber tube; this is inserted in a large rubber tube having an outside diameter of 18 mm. With a finger cot over the end, this applicator is inserted in the rectum and left in from four to six hours.

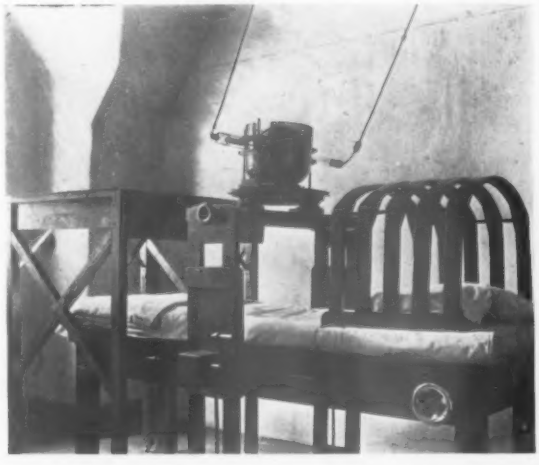

FIG. 2. High-voltage treatment table showing the cradle at the right, and high table at the left, for holding the protecting lead rubber above the patient. Two small strips, only, are placed directly upon the patient.

In women I also give a vaginal radium treatment.

The roentgen treatment is given at 200,000 volts, with 0.5 mm. Cu. and 1.0 mm. Al. filtration, and 20-in. target distance. At 4 ma. a total of three hours is given in the average case, equally divided between the anterior and posterior aspects of the pelvis. A leaded rubber strip is placed below the pubes and another about 10 in. above and the entire pelvis exposed between these two.

[1] SIMPSON, F. E. Radium Therapy. St. Louis, 1922, p. 211.
[2] CABOT, H. Modern Urology. Philadelphia, 1918, ii, 238.

In a heavy patient a slightly longer exposure is given, by additional anterior treatment.

A second course of treatment is given six to ten weeks afterward, if necessary, and the dosage is varied according to the amount of reaction produced. Epilation and erythema are considered necessary for the best results. If two series of radiations do not cause complete disappearance of the tumor, fulguration is advised. Geraghty[1] found that "some papillary tumors which seemed extremely resistant to fulguration treatment responded very promptly after a small amount of radiation. Consequently it has been a habit in our clinic to radiate most tumors, even those which subsequently will be treated by fulguration."

CONCLUSIONS

The best treatment of bladder tumors is a combination of radium and high voltage roentgen rays. I fully agree with Jenkinson, of Chicago, that "some of our best results with the deep roentgen therapy have been in urinary bladder tumors."

A CASE OF TUBERCULOSIS OF THE SYMPHYSIS PUBIS

BY J. B. JACKSON, M.D.

KALAMAZOO, MICHIGAN

DISEASE of the symphysis pubis appears to be relatively very rare. Obstetricians refer to an occasional septic process in this joint following trauma during labor. On account of the structure of the joint it is comparatively free from the acute infections.

The symphysis pubis belongs to the type of articulating surface known as amphiarthrosis. This type of articulation admits of a very limited range of movement. The joint contains no true synovial membrane. The articular surfaces of the pubic bones are covered with a thin layer of hyaline cartilage. Between these lies a disc of cartilage and fibrocartilage. The joint is securely held on all sides by ligamentous bands. The anterior and the sub-pubic ligaments are the more important of these structures. The joint structure is similar to the sacroiliac joint and to the articulation between the vertebrae.

Tuberculosis of the spine is a comparatively frequent manifestation of tuberculosis. Tuberculosis of the sacroiliac joint is observed infrequently. Tuberculosis of the symphysis pubis seems to be a very rare disease. A review of the literature brings out the fact that before the general use of the *x*-ray the diagnosis was extremely difficult. We have been unable to find any report of tuberculosis of the symphysis pubis in English, although the possibility of its occurrence is mentioned briefly by various authors.

The condition was apparently first described by Hennies in 1888. He reported 3 cases, 1 male and 2 female. They were all treated surgically and all recovered. He states that the pain in this disease is easily mistaken for neuralgia and the tumor for hernia or a psoas abscess.

In 1890 Chauvel reported one case of a man aged twenty-three. In this case almost the total of the symphysis pubis was involved and necrotic and was removed in the form of sequestra.

Von Bungner in 1899 reported a case in a woman aged fifty-seven. This case was treated surgically and recovered. He refers to the danger of mistaking the abscess for inguinal hernia. He states that the prognosis depends upon tuberculous lesions elsewhere in the body and on the use of early radical surgical treatment.

In 1902 Herz reported 2 cases. In this article he states that Krause has briefly mentioned 2 cases. Herz's 2 cases were males aged eighteen and fifteen. Both were treated surgically. One died. This death was attributed to the fact that the patient would not consent to the operation until extensive destructive processes had taken place. The other made a good recovery. He mentions difficulty in walking as an early symptom. Krause noticed

[1] GERAGHTY, J. T., Treatment of malignant disease of the prostate and bladder. *J. Urol.*, January, 1922, vii, No. 1, p. 46.

in his 2 cases an abnormal motility of the pelvic bones.

Tillman in 1905 writes of the rare occurrence of tuberculosis of the symphysis pubis. In addition to the cases already mentioned in this review he mentions a case reported by Motz in 1890. Tillman refers to the formation of cold abscesses above and behind the symphysis. Pus may collect in the inguinal region. Fistulae usually occur above the horizontal ramus on one or both sides; more seldom in the middle or both sides of the labia majora or scrotum or on the inner side of the thigh below Poupart's ligament. He speaks of disturbance in the gait as an early symptom. According to this author, prompt and early surgical treatment is the only treatment worthy of consideration.

Woloch in 1907 reports in detail a case in a woman of sixty-three who finally recovered following extensive surgical treatment. He states that because of the paucity and indefinite character of the symptoms the cases are seldom diagnosed until the appearance of fistulae. He mentions the possibility of involvement of the hip by extension along the pelvic ramus and the perforation of the bladder by the abscess.

Bungner in 1914 reported a case in a woman of fifty-seven treated successfully by surgery. He considered the disease more common in women than in men. In all cases described suppuration has occurred. Dry caries has not been described.

Rendu and Wertheimer in 1922 reported a case of tuberculosis of the pubis and symphysis in a boy aged nine. There was a fluctuation over the internal part of the right thigh. Radiography showed a bone lesion in the descending branch of pubis at angle of pubis. At operation the symphysis was found involved. There was complete recovery following curettage.

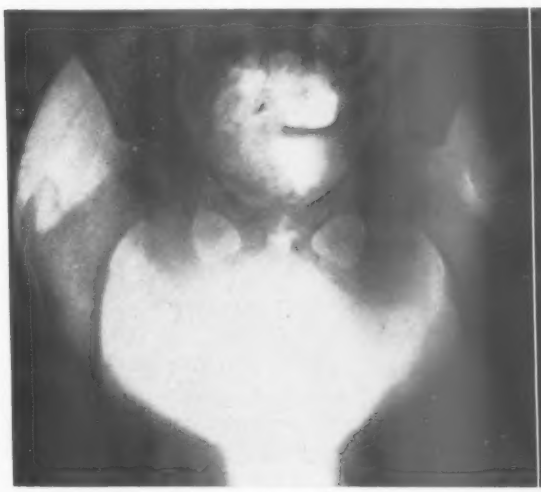

FIG. 1. Apr. 10, 1922.

FIG. 2. Jan. 13, 1923.

During the present year (1923) Swynghedauw and Druon have published a paper on this subject. They state that tuberculosis in the pubis is particularly insidious and is only revealed by fistulae generally appearing considerably distant from the affected spot. In the majority of cases the diagnosis was for a long time erroneous; and by radiology alone was the true condition revealed. They state that in 1916 Bessett collected 56 cases, but that several of these were not truly cases of tuberculous osteoarthritis. They mention 9 cases since that date and 1 case seen by themselves. Pregnancy and labor are undoubtedly factors in several cases. Under the influence of labor a previously latent lesion becomes acute and in several cases has led to the patient's death. However, the disease is slightly

more frequent in males. They refer to Labeyre's description of a periostitis of the pubic region characterized by a thickening and caseous transformation of the periosteum. This type has a tendency to invade the angle of the pubis and spread to the symphysis, the cartilage of which ulcerates, softens and then peels away; fungosities are soon substituted for cartilage, the ligaments are resorbed and the symphysis stripped of all means of contention and destined to rupture on the least effort.

FIG. 3. Mar. 23, 1923.

Surgery is especially valuable in the treatment because of the fact that the symphysis pubis is superficial and easily accessible. These authors think, however, that in early cases without pain, suppuration or sequestra, operation is not justified, and that such cases only call for the general treatment of tuberculous osteoarthritic lesions.

We should like to report the following case in which the diagnosis was made in the course of a roentgenological examination of the lumbar spine:

The patient is a girl who was first seen in February, 1922. She was at the time eleven years old. She had never been robust. She had had measles, chickenpox and a severe attack of whooping-cough. Two years previous she had had influenza followed by pneumonia. About a year ago she had a severe colitis which lasted about ten days. There is no family history of tuberculosis. The father and mother are living and well. She has a brother about a year younger who is described as "frail."

A few weeks before she was first seen by us, the family had noticed something unusual about the gait. There was difficulty about walking fast or running. Soon after this a swelling was noticed on the anterior surface of the right thigh immediately below Poupart's ligament. At this time she was brought for *x*-ray examination

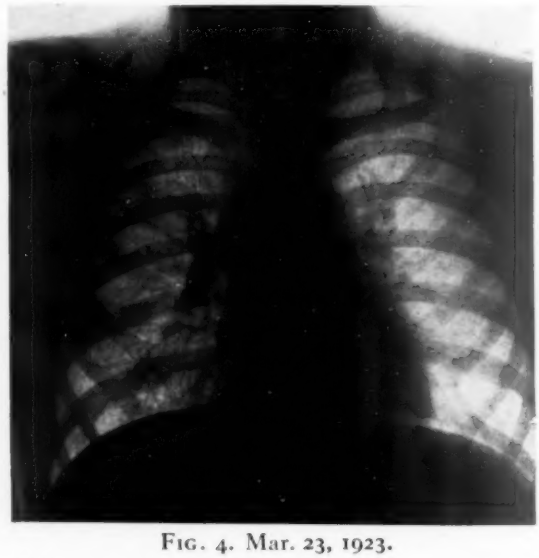

FIG. 4. Mar. 23, 1923.

of the spine where the abscess was supposed to have originated.

The *x*-ray examination of the spine showed no evidence of vertebral disease. On the films made of the lower spine there was observed a destructive lesion of the pubic bones at the symphysis pubis. This first called attention to the symphysis pubis as the site of the lesion. Further *x*-ray study was then made of this region. The cold abscess was aspirated. About one and one-half ounces of a thick, creamy, greenish pus was withdrawn. Cultures made from this were sterile. A guinea-pig inoculation with the pus resulted in an extensive tuberculous infection at the end of twenty days.

A set of stereoscopic plates was made on April 10, 1922, with the patient in the prone position. There is a honeycombed appearance of the body of the pubis on the right side which extends well into the

horizontal branch of the pubis and down to the lower border of the symphysis. On the left side there is also a honeycombed appearance of the body of the pubis, much less extensive than on the right. There is apparently some separation of the two pubic bones. No thickening of the periosteum can be made out, the bone lesion being apparently a destructive process with no tendency to production of new bone.

Another set of stereoscopic plates was made on January 13, 1923, with the patient in the prone position. The lesion has apparently been somewhat progressive. The honeycombed appearance on the right side extends slightly further back. There is very much less bone detail to be seen at the site of the lesion. The fine reticula of bone seen in the first plates have apparently been destroyed by the progress of the disease. The destructive process on the right side is considerably more extensive than that on the left. At one point near the lower border of the body of the pubis the obturator foramen is nearly broken through. There is still no evidence of bone proliferation.

The last set of stereoscopic plates was made on March 23, 1923. There is apparently no further extension of the disease. There has been further destruction of the bone, so that there is almost no bone detail to be seen between what is left of the two pubic bones. The diseased bone apparently has been gradually destroyed, but there has been no appreciable advance in the extent of the lesion.

On March 23, 1923, a set of stereoscopic plates was made of the chest with the patient in the prone position during full inspiration. The shadow of the heart and great vessels is normal. There is no fluid in either pleural cavity. The costophrenic angle is normal on each side. There is apparently no thickening of the pleura over the apex of either lung. The hilus shadows are rather large and nebulous and show very little tendency to calcification. From the right hilus extending up toward the first and second interspaces in front are very dense peribronchial lines which lead to the periphery of the lung. On the right side there is some peribronchial thickening extending up toward the apex and the first intercostal spaces. The peribronchial lines on the left side are less dense than on the right. The thickened bundles of peribronchial lines seen extending from the right hilus towards the first and second interspaces very strongly suggest old pulmonary infection.

The treatment carried out by the child's father, a physician, has been non-surgical. The child has not been allowed to walk. No immobilization apparatus has been applied. Especial attention has been given to nutrition, fresh air and sunshine. Of late, exposure to direct sunlight has been used.

She was last seen by us in March, 1923. The cold abscess refilled slightly after aspiration but there was a very little swelling when she was last seen. There has never been a discharging sinus. The temperature has shown very little tendency to elevation. She has gained several pounds in weight and feels perfectly well.

The infrequency of this condition has seemed to warrant our report of this case. It is too early to judge of the result of treatment, but the case seems to be doing fairly well. We are mainly interested in the *x*-ray study of the case and wish particularly to call attention to the possibility of tuberculous caries of the symphysis pubis when searching for the origin of cold abscesses or fistulae in the region of the pelvis.

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ROENTGEN THERAPY OF CHRONIC PROSTATIC HYPERTROPHY*

BY J. THOMPSON STEVENS, M.D.

MONTCLAIR, NEW JERSEY

IN Cunningham's Anatomy one can find the following statements: "In old age the prostate frequently undergoes an hypertrophy which may affect chiefly the glandular tissue, or the entire organ. Not infrequently calcareous concretions are found imbedded in the prostate. In old people the veins of the prostatic plexus usually become much enlarged." Add to the above the chronic, passive inflammation that is present in many of the cases of prostatic hypertrophy and we have the complete pathology or the physiologic pathology of the usual case of simple enlargement of the prostate gland.[1]

We have for years known that glandular tissue is the easiest normal tissue of the body to destroy by means of the roentgen rays or by radium rays. For example, when raying about the mouth, the operator is often greatly annoyed by the complaints of dryness of the mouth and throat. This complaint is due to the radiation which is sent into the depth of the salivary glands. Under proper methods of technique this complaint is only temporary, but with greater dosage would become permanent because the salivary glands would be destroyed. Again when raying the depths in the region of the suprarenal capsules, it is, I believe, good technique to give the heaviest doses of rays from the front with lighter doses from the back and sides, also to prescribe feeding of suprarenal substance to overcome the untoward effect of the rays upon the suprarenal capsules.

It is a proven fact that radiations in proper amounts will cause endarteritis and phlebitis resulting in a reduction in the size of the arteries and veins, thereby causing a reduction in the amount of blood entering and leaving the region that has been radiated. Continued radiation would eventually cause an obliterative endarteritis and phlebitis. For example, I will just mention the promptness with which uterine bleeding stops under treatment by means of radiation therapy, whether the hemorrhage is due to carcinoma, to fibroid, or is idiopathic.

From what has already been said about the pathology or the physiological pathology as encountered in the usual case of simple hypertrophy of the prostate gland, that is the hyperplasia of the glandular elements, the enlargement of the veins of the prostatic plexus, and the chronic inflammation, one must admit the possibilities for treatment by means of radiation therapy.

The results following roentgen therapy in chronic prostatic hypertrophy have been so uniformly good that I feel justified in presenting these few cases for your consideration.

Up to the period ending July 31, 1922, 33 cases of hypertrophy of the prostate gland have been treated. No case was refused treatment and every means was exhausted to make the best possible diagnosis. In each instance the diagnosis was made by a medical man or surgeon in addition to my own studies. Out of the total of 33 cases there were 9 catheter patients, 24 who complained of one or more of such symptoms as frequent micturition; urgent, painful urination; nocturnal, frequent urination; hematuria; pain in the perineum; strong-smelling urine etc., and who upon examination showed a definite tumor in the prostatic field and residual urine. The tumors varied in size and were generally about as large as would be expected with the symptoms presented by each patient. The largest gland felt very much like the head of a child presenting at term. It was in this case that we obtained one of our best results, the details of which are given below, in fact the gland was so large that the patient, in addition to having to use the catheter, was beginning to have considerable trouble in emptying his bowels. Out of the 33 cases we have to date one

[1] STERN, SAMUEL. *X*-ray treatment of hypertrophy of the prostate. AM. J. ROENTGENOL., June, 1921, viii, 292.

* Read at the Midwinter Meeting of the Eastern Section of THE AMERICAN ROENTGEN RAY SOCIETY, Atlantic City, N. J., Jan. 25–27, 1923.

failure and two deaths. The failure was in one of the catheter cases who presented one of the largest prostatic tumors that was treated. This case too, I have cited in detail below. Death was due in one case to cerebral hemorrhage and in the other to cardiac failure. In 30 out of the 33 cases our treatment met with success, i.e. the retention was relieved, likewise the frequency, the urgent, painful urination, the bleeding, the pain in the perineum etc.; and upon examination it was found that in 3 of the cases the gland had returned to normal size, and that in 27 cases it was reduced on an average to one-third its size as determined in the beginning, and instead of being hard, was soft to the touch.

Case I. Male, a patient of Dr. T. Paczkowski, aged sixty-two, unemployed; sent for treatment Sept. 7, 1920. For a considerable period of time he had complained of frequent, urgent micturition. At night he would commonly try to pass his urine about every ten minutes. For the past two months he has been unable to pass any urine at all unaided, and required catheterization twice daily. Lately he has noticed a sensation of weight in the perineum and it is becoming quite difficult for him to have a satisfactory stool.

Examination shows an old man upon whose face there are unmistakable signs of pain and misery. A metal catheter brought away one and one-half quarts of urine. (I was unable to get the usual soft rubber catheter into the bladder.) Rectal examination shows a mass in the prostatic field which feels much like a presenting vertex at term. The mass appears to be symmetrical and is very hard and tender. General physical condition of patient is excellent.

Treatment. Eight areas for application of the roentgen rays were used, four just above the symphysis pubis, two over the gluteal muscles to the right and left of the anus. Over each area the rays were centered toward the prostatic field. Factors for treatment were: 5 ma., 133,000 volts crest value, 8-in. focal distance, 6 mm. aluminum filter, and time sufficient to give $\frac{1}{5}$ of an erythema dose over each area. Time will vary with different machines—in fact it varies in my office between two machines of exactly the same construction. These treatments were repeated in October and November for prophylaxis.

Results. The third day following our first treatments the patient emptied his own bladder and has not had to be catheterized since. One week after treatment there was a bloody discharge from the bladder together with many small stones. Bleeding and passage of stones has to date been present but once as just outlined. Rectal examination two months after treatment was completed showed a total absence of any tumor in the prostatic field. Upon inquiry through Dr. Paczkowski, I find that there has been no recurrence of any bladder symptoms. Our patient has been well for two years and four months since treatment was started by means of the roentgen rays.

Case II. Male, a patient of Drs. W. E. Doremus and J. G. Cottrell, aged seventy-three sent for treatment March 14, 1922, with complaints of dribbling and frequency which had been present for the previous four or five years. The frequency was most marked at night and in the winter. For the three weeks before he was referred to me, he had been unable to empty his bladder except by catheter. Ten days before the catheter had to be used, there was an attack of bronchopneumonia.

Examination shows a weak, tottering old man hardly able to walk unaided. The prostate is large and soft. Dr. Doremus once found the upper border of the bladder on a level with the umbilicus. Catheter brought forth purulent urine. Phenolsulphonephthalein test gave a 10 per cent total for two hours.

Treatment. Four areas were selected for the application of the roengen rays, two over the symphysis pubis and one to the right and left of the anus over the gluteal muscles. Over each area the rays were centered toward the prostatic field. Factors for treatment were: 5 ma., 133,000 volts crest value, 16-in. focal distance, 6 mm. aluminum filter, and time sufficient to give $\frac{1}{5}$ of a full dose over each area. These treatments were repeated on March 30, 1922 and April 14, 1922.

Results. During our treatments the patient became able to empty his bladder once daily when on his back. He had to be

catheterized once daily and was unable to pass any urine when standing. Why this should be so, I am sure I do not know. There was marked improvement in the patient's general condition, and he walked alone with a quicker, firmer step. In any event our treatment failed to eliminate the use of the catheter and in no way relieved the desire to urinate. On June 19, 1922, Dr. Doremus found that the phenolsulphonephthalein test now gave a total excretion of 50 per cent, that is, nearly a normal result. This with other findings led to a decision to remove the gland surgically.

Operation. Suprapubic removal. June 23, 1922. Dr. Doremus reports that the gland was removed with very little loss of blood, and the surgical difficulties were no greater in this case than in others, which had not been treated preoperatively by radiation therapy. Operation was followed by an attack of bronchopneumonia, and during a spasm of coughing the suture line burst open. Then followed a hernia of the peritoneal pouch and bladder wall through the opened suture line. Under local anesthesia, on Nov. 28, 1922, the redundant or excess membrane was removed and the skin closed with a good result except that there is still a draining suprapubic fistula of pin-point size. A No. 26 sound drops into the bladder, thereby eliminating any uretheral obstruction which might keep up the drainage.

Results. Ever since the prostate was surgically removed the patient has been able to pass his urine freely and the general health is excellent.

Laboratory Findings. Whole gland was removed and weighs 52½ gr. Section shows several cysts filled with a thick greenish material. Fibrosis very well marked. The microscope shows glandular elements markedly increased, stroma shows increased fibro-elastic tissue. Diagnosis: Adenoma with fibrosis. No evidence of malignancy.

Remarks. The reason why we failed to produce the desired results by means of radiation therapy in this case, is evident to every radiotherapist. None of us treat cystic goiter, because our treatment accomplishes nothing. Cystic goiter is usually easy to diagnose, but I know of no method of examination that will diagnose a cystic prostate in the living patient. Also we are unable to influence fibrous tissue without destroying surrounding normal tissue. In other words, I shall always believe that this case was a failure because of the cystic disease with fibrosis.

TABLE

	Total No. of patients treated	No. of successes	No. of failures	Percentage of successes	Deaths	Percentage of deaths
Catheter patients	9	8	1	89	0	0
Patients with bladder symptoms, enlarged prostate, and residual urine...	24	22	0	92	2	8

CONCLUSIONS

1. If the results obtained in this series of cases can be produced in the majority of cases that present themselves for treatment in the future, the treatment of simple hypertrophy of the prostate gland by means of radiation therapy is justifiable. These old, debilitated men will appreciate this method of treatment.

2. In proper hands the treatment is free from danger.

3. There is no loss of voluntary control of the bladder, likewise the rectum is not injured, there is no persistent urinary fistula, and complicating conditions are usually no contraindication to radiation therapy. The treatments are given without shock, hemorrhage, uremia, bronchitis, septicemia, pulmonary embolism, etc., and there is no mortality that can be traced to the treatments for a cause.

4. Should treatment by means of radiation therapy fail, surgery can be substituted. Radiation does not produce any condition which interferes with surgical removal of the gland. In fact, in our one case, following radiation the gland was removed with much less hemorrhage and without more surgical difficulty than had the patient not been radiated.

DISCUSSION

DR. PFAHLER. I believe myself that this is a field that has been very much neglected. I have not treated many cases, but at least the

patients whom I have treated have improved symptomatically in all cases. Perhaps it was the natural course of events.

Originally I carried out a technique very much like that used by Dr. Stevens, but I do not believe it is a technique we will follow in the future when we do treat these patients. I think we will treat at long distances and probably confine the treatment to the perineal region. We need never go to the extent of damaging the skin.

Some of you may know that I am treating with high voltage with the tube under a 16-in. concrete floor, and therefore I have considerable distance even to start with, and the closest I get to the patient is 62 cm. I have constructed a special chair to fit on the floor so that the patient sits rather comfortably on the floor and the rays are sent up through the perineal region and are confined to the region of the prostate. My aim has been, with the high voltage and highly filtered rays, to give about 50 per cent of an erythema dose and repeat it perhaps once a month. In that way is brought about a progressive but positive atrophy. It may be just the natural course of events.

Dr. Stern. Unfortunately I did not hear all of Dr. Stevens' paper. The part I heard dealt with his technique and his final results, and it gave me a great deal of pleasure to hear of them.

Some years ago I read a paper at one of these meetings here on the *x*-ray treatment of hypertrophy of the prostate. At that time I quoted 6 or 8 cases that were very much improved. These patients have all kept well and in not a single case has surgical interference become necessary. Since that time I have treated quite a number of others and the results in most of these cases were very gratifying. I have not been able to do much for patients who have already entered the catheter life. They reach a point of improvement where most of their subjective symptoms are improved, but they still have to keep on using the catheter. I think this is due either to a mental hazard on their part, that is, they just feel that they cannot voluntarily void, or there is a paralysis of the sphincter through disuse, which makes it impossible for them to regain control.

My technique seems to differ from Dr. Stevens'. I do not treat them through the symphysis, for the simple reason that working with a low voltage and 6 mm. Al. filter, there is a long distance to travel to reach the prostate and the depth dose from an exposure given this way is rather small. When I was abroad I found that they were treating these cases with high-voltage intensive treatments. In one case in which I tried this, the treatment produced considerable tenesmus of the bladder and made the patient so uncomfortable that I decided to continue with my low-voltage fractional treatment. With my technique I use the rectum and the perineum as my ports of entry. I give them one-half of the erythema dose filtered through 4 mm. Al. once a week through the rectum and through the perineum. Four of these treatments constitute one series. Treatment is repeated at the end of a month's interval and again after an interval of one or two months following this. Cases that have a cystitis must be treated for this separately in the usual way. The symptoms of hypertrophy of the prostate and cystitis are so similar that no matter how much we improve the condition of the prostate, with a persistent cystitis, we still get practically the same symptoms as we did before. The treatment is so simple and the majority of these patients do so well that I see no reason why it should not be tried on all prostatics before surgical interference is advised. The amount of ray that they receive would not in any way interfere with carrying out surgical measures if the treatment should fail.

These cases, a great many of them, if referred to us in their earlier stages, I have no doubt would be saved an operation.

Dr. Hunter. In 1911 I presented a paper on this subject at the Richmond meeting of the American Roentgen Ray Society. I thought I got some fair results.

I would like to ask Dr. Stevens one or two questions: I used to treat these cases in the Sims position and treat through the perineum. I had a feeling at that time that application of rays against the scrotum did have some effect; perhaps I was influenced by the surgical opinion in which a double orchidectomy was considered as helping prostatic conditions.

I feel now that with the filter and long distance we should accomplish a great deal. Just after my paper the two-stage operation for prostate was introduced and the result was that the surgical mortality fell to its present rate.

I would like to ask Dr. Stevens what he thinks of treating through the perineum, especially with the new technique and using a rather large area, and whether he thinks direct application of ray to the scrotum has any advantage at all.

Dr. Stevens (closing discussion). In 3 of the cases in our series the prostate was reduced in size enough to give no residual urine. In the others, the average amount of residual urine remaining after treatment was about one-third of that before treatment. The first case reported above in detail was the most striking

result obtained in many respects. This was the only case in the entire series suitable for surgery. The others were in such condition that surgery could never have been instituted with any hope of their living through the operation.

The pathology of the usual case of prostatic hypertrophy would naturally lead the radiotherapist to the conclusion that such cases belonged to him. Surely if he had a disease with chronic inflammation, with enlargement of veins, or with hyperplasia of glandular elements, he would be justified in expecting his treatment to produce nearly perfect results.

I am rather disappointed in what Dr. Stern had to say about the treatment in Germany with the higher voltage rays. Having been equipped with the necessary apparatus for higher voltage work in 1922, I had hoped to be able to work out a definite therapeutic dosage for the treatment of hypertrophy of the prostate. Dr. Stern's discussion, I feel, answers Dr. Pfahler's discussion. Dr. Pfahler apparently was looking hopefully to the higher voltage rays to produce even better results in the future. I am of the same opinion regarding the higher voltage rays. Before we can speak with authority they must be tried out extensively by several of us.

In reference to surgery after radiation, in the one case I reported in detail which did have surgery, the surgeon said that the operation was done with very little bleeding, also that the difficulties of surgical removal of the gland were not increased.

Dr. Hunter's work with no filter must have been done long ago when little was known of the proper methods of getting high intensity depth doses. With no filter we would get a high dose of rays on the skin very quickly with little or no depth intensity, therefore without beneficial results. I have had no experience in the treatment of this condition by exposure of the testicles. I have always been very careful to see that they were not exposed to the rays.

ROENTGEN-RAY TREATMENT OF THE THYROID

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DURING the past five years roentgenotherapy in the management of toxic thyroids has been steadily gaining recognition. There are certain cases which are definitely surgical, and others which are just as definitely cases for the internist and roentgenologist. Experience has taught us that the colloid, cystic and simple goiters with no toxic manifestations are not suitable cases for roentgenotherapy. Thyroids causing pressure symptoms are definitely surgical. Toxic adenomata should always be given the benefit of *x*-ray therapy before being subjected to surgery. If, after careful and proper treatment, the *x*-rays fail to produce a marked improvement, surgery may be resorted to. The number of failures, however, under roentgenotherapy, if properly administered, will be small.

The question of adhesions following *x*-ray therapy is often raised by surgeons. Some surgeons claim that following its use, operation becomes very difficult, due to the large amount of hemorrhage and connective tissue encountered. On direct inquiry, the majority of surgeons questioned have stated that they experienced no great difficulty in removing the gland. One case is illustrative: a woman of twenty-four, suffering from an exophthalmic goiter, had been given six series of *x*-rays and her condition did not improve as rapidly as the internist had anticipated. The patient being a working-girl, and time being an important factor in her treatment, it was thought advisable to resort to surgery. The operation was comparatively simple, for the gland was removed without any difficulty. No increase in connective tissue was found, and there was no increase in the amount of hemorrhage

Physicians using roentgen therapy in the treatment of toxic thyroids are often asked: What are you using on your thyroids? What voltage? What filter? What milliamperage? etc. After treating and watching about 300 cases, we are convinced that the administration of the *x*-rays must be according to the individual case. Its use as a therapeutic agent must not be a fixed quantity from which no deviation shall be made. It is a matter of judgment and cannot be made to conform to a simple rule of

thumb. A thorough physical examination is indispensable, the heart and nervous system being closely scrutinized. Rest in bed is imperative, before and after treatment, preferably in a hospital. The patient must be made as comfortable as possible. The nurse caring for the patient should at all times be agreeable, for these patients are very irritable and easily upset. Each time the patient becomes nervous and irritable, a definite setback is the result. The food should be very nourishing and easily digested. Drugs may also be used in conjunction with the *x*-rays; the bromides

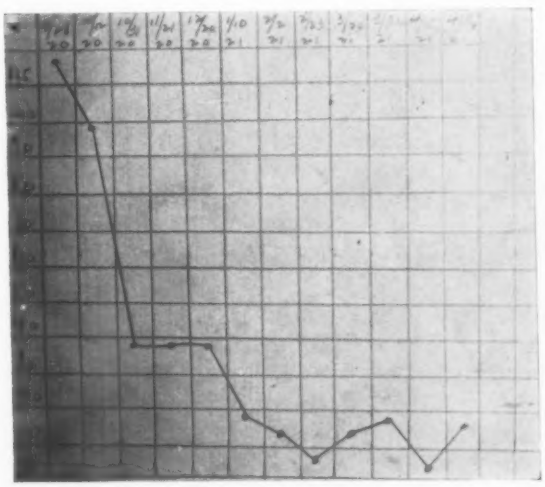

FIG. 1. Case 1. Five series of *x*-rays. Gained 55 lbs. Symptom-free.

have a tendency to lessen the nervousness. An ice bag to the precordia, in some cases, is helpful. During the series of treatments the bowels should be regulated by the use of bland cathartics or an occasional enema.

For radiation sickness, which sometimes occurs, one dram of sodium bicarbonate in cold water may be given three times a day. A good plan is to put the patient on bicarbonate of soda two days before starting the treatment, continuing through the series.

The treatment room should be very quiet and well ventilated. The use of electric fans tends to keep up a good circulation of air, lessening the chance of radiation sickness. The transformer should, whenever possible, be in a sound-proof room. The testing of the machine, obtaining the spark-gap and milliamperage should be done before the patient arrives. All unnecessary noises and handling should be avoided. All patients should be transported to and from the treatment room on a stretcher. If the above details are complied with, the amount of nervous reaction is lessened. During treatment, the patient should be made comfortable, assuring her that she will experience no pain. She should be instructed that quiet is necessary during the exposure, and that the procedure is devoid of any danger.

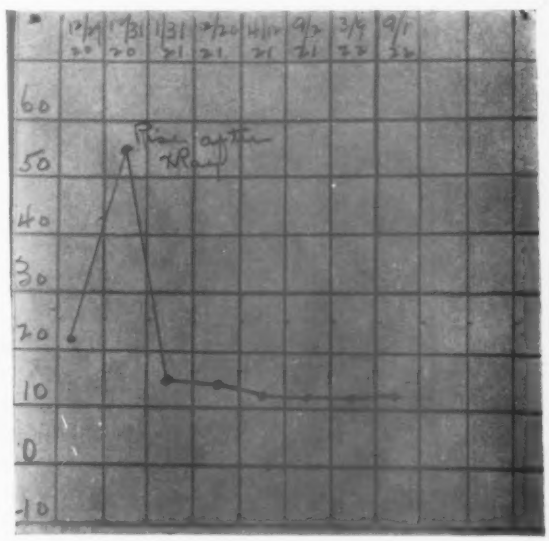

FIG. 2. Case 2. One series of *x*-rays. Recovery complete.

After a careful consideration of the individual patient, the size of the dose is estimated. If the patient is very toxic and shows a greatly increased metabolic rate, one treatment is given over the thymus anteriorly. The patient is then allowed to rest for a day before administering another treatment, and the effects of the treatment are observed. Subsequent dosage should be modified according to the reaction experienced after the first treatment. There is no particular hurry in giving the treatments; in fact, the patient will usually do better if kept in the hospital a week for the series.

In treating goiters, three areas are given through portals 4 × 4 in. The thymus is rayed anteriorly in all cases. The thyroid is treated through two portals, one to each lobe. The larynx is carefully protected during treatment. In no case is an attempt made to obtain a skin reaction. If an

erythema, or even repeated tannings are obtained, a subsequent telangiectasis is apt to occur.

In all cases a comparatively heavy filter of 6 mm. of aluminum is used. A 12-in. focal skin distance is a constant factor, also 5 ma. The voltage in all cases is 125,000 peak, or the equivalent of a 9-in. spark-gap between points. The time is the variable factor and is changed to suit each case.

Following the treatment, in the course of twelve hours, the thyroid may show a marked enlargement. The patient or relatives may call you, complaining of the swelling of the neck; you can assure them that nothing serious will follow and that in another twelve hours the swelling will have subsided.

For the past eighteen months, a basal metabolism has been determined on all cases prior to treatment, and repeated following it; this has lessened the chance of going too far in the treatment, producing a hypothyroidism. Before a second series of treatment is administered, the patient is instructed to return for a physical examination and a determination of the metabolic rate.

It has been our policy not to treat a patient after the metabolic rate has dropped to +15. A few cases have been treated when the metabolic rate had reached a slightly lower level, but never when lower than +10.

The clinical manifestations usually coincide with the metabolic rate. Patients having a metabolic rate of +80 to +90 should by no means be subjected to the same treatment as patients with a +30.

The dose of the *x*-rays indicated in each case is decidedly different. If a patient with a metabolic rate of +90 were given the same dose as the patient with a metabolic rate of +40, the results would, in a great many instances, be unfavorable.

The heart action in many cases becomes more rapid; nausea, vomiting, severe headache, and occasionally collapse, follows. Delirium was observed in three cases.

The above observations are mentioned to emphasize one point: *Treat the individual case.*

Many cases, showing some of the symptoms of a toxic goiter, are referred to our department for *x*-ray therapy. These patients are subjected to a metabolic test before deciding upon the type of treatment to be followed. Frequently the metabolic rate is found to be normal. Such cases are always re-examined to rule out any error in the determination. If, after the second examination, the results are the same, the patient is not radiated but carefully watched, and the test repeated at short intervals. Many cases showing symptoms similar to those encountered in hyperthyroidism are suffering from pathology located outside the gland. There are times when even a hyperthyroidism will show a comparatively low, or even normal metabolic rate. It will be observed, however, that during the period in which the metabolic rate is low, the symptoms will also have subsided. If these patients suffer an exacerbation, there will be a concomitant rise in the metabolic rate.

Criticism of the basal metabolism, belittling the method and attaching very little significance to its value, is in many instances unwarranted. If the test is made during a period when the patient is absolutely quiet, as the word "basal" implies, the results will be of great value in determining the severity of the disease. The fact that the test must be in some cases repeated before a definite rate can be established, does not in any way lessen its importance. We are all called upon, in many cases, to repeat physical examination of the heart and lungs, before arriving at a definite diagnosis. Even the surgeon must at times repeat the operation for hernia, before a cure can be obtained.

The close cooperation of the surgeon, internist and roentgenologist, similar to the plan adopted at the Massachusetts General, will certainly bring about a better understanding of the various methods of treatment, from which the general public will profit. It seems that we are all carrying a chip on our shoulder, each claiming that his method is the only one that will produce a cure. If we worked in harmony this feeling would not exist, and the results in many cases would show a higher percentage of cures. I am quite sure the *x*-ray will not

cure all cases of hyperthyroidism, and I am also convinced that surgery has a certain number of failures.

In many localities, a compensatory hypertrophy of the gland is endemic. This is a physiological process and should not be interfered with. The presence of a rapid pulse or even of a tremor in such cases, is not conclusive evidence of an exophthalmic goiter or hyperthyroidism. We do not believe an exophthalmic goiter or hyperthyroidism is ever encountered with a metabolic rate constantly normal or below. In deciding these cases, the basal metabolic rate is of great value.

Approximately 100 cases have been checked immediately following radiation. In all of these there was a marked rise in the metabolic rate. The average rise was about twenty points. The cases showing the highest rates usually showed the largest increase; one patient, however, showing a low reading of +18, increased to +50 immediately following the series. Accompanying the rise of the metabolic rate, there is a proportional increase in the severity of the symptoms. We can see from the above findings that each case is a separate and distinct entity.

In the series of 300 cases the results have been uniformly good. With the exception of 2 patients, there has been a marked improvement in all cases. This does not mean, however, that all our patients were cured.

Two fatalities occurred in our series. At present, we do not feel competent to discuss the cause of death. Autopsies were not obtained in either case. The *x*-ray dosage in both cases was very small and distributed over a period of ten days for the one series. Both patients had been treated before, and nothing unusual was noted during the previous series.

In this series, one patient showed a metabolic rate of +150, accompanied by all the classical symptoms of a toxic thyroid. After four series, the recovery was complete, and during three years' observation there has been no return of symptoms. The metabolic rate has remained normal.

CONCLUSIONS

1. Not all types of goiter are amenable to *x*-ray therapy. The colloid, cystic and simple thyroids should not be subjected to radiation.

2. Each case should be treated as an entity. Routine treatment of all cases is unsatisfactory.

3. Frequent metabolic determination is an indispensable guide in the treatment of thyroids.

4. The majority of cases of hyperthyroidism and exophthalmic goiter will respond to *x*-ray therapy.

CLINICAL PROBLEMS IN ROENTGEN THERAPY OF DEEP-SEATED MALIGNANCY

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A PERUSAL of the current literature must undoubtedly lead the uninitiated to the conclusion that the application of the roentgen rays for therapeutic effect is now merely a problem in physics; that one need only apply a certain percentage of a given dose to a specified volume of tissue to produce good clinical results. Such a conclusion is, of course, a most erroneous one. Deep therapy, as the name implies, was elaborated in an effort to influence deep-seated malignant lesions, but the efficient treatment of such conditions means much more than the application of a calculated dose to the primary seat of the trouble. The patient coming to the radiologist for treatment is usually well beyond the early stages of his affliction and presents symptoms of a varied nature, based upon one of many intricate combinations of pathological lesions. He is, unfortunately, quite often sent to the roentgen laboratory only after all other methods have failed. Treatment should be planned to give symptomatic relief, especially where a complete cure is improbable. It is first necessary to take a careful history and carry out a most thorough and searching physical examination. The data obtained should be filed in permanent form in the laboratory, for without such data no intelligent idea of clinical progress is possible. Information obtained from careful examinations made at regular intervals following the irradiation should be filed in the same record. It may seem unnecessary to mention such examinations, and yet there are many laboratories in which they are not made, and many of the case records are extremely meager except as regards physical data. We have seen patients receive treatment in a cut and dried manner without the removal of any of the clothing, the plan of attack being a routine one for the diagnosis sent in.

Certain radiologists have contended that their patients should be examined by a clinical man because they themselves are not capable of making the necessary investigations. If these men would take up the study of the clinical course of malignant tumors and add the information gained to their extensive knowledge of the roentgenographic appearance of malignancy in the chest, bones, stomach, colon, kidneys, etc., they would be much better prepared to examine cases of malignancy than the average clinical man, who considers cancer as only one of the branches of his work. This paper is written in an effort to turn some of the energies of the roentgen therapist from the field of pure physics to the great realm of gross pathology and biological reactions; for after all, we are treating living patients and not tanks of water having a depth of so many centimeters.

It is not our purpose to belittle the importance of the recent progress in *x*-ray physics, but rather to insist that the clinical side of the work be given its proper consideration. At least two problems should be considered before the matter of depth dose is touched upon. These are: First, the sensitiveness of the normal structures to be rayed, and second, the nature and distribution of the malignant cells to be attacked.

Accurate data relative to the vulnerability of the internal structures is quite meager. We know that the mucous membranes of the gastrointestinal tract, the bladder and the trachea are relatively quite sensitive. Injuries observed in the intestines of experimental animals are described by Martin and Rogers.[1] Wintz[2] states that ulcers in the mucosa were observed in his pelvic cases. Evidence has also been brought forward suggesting that the pulmonary tissues may be injured. Intrathoracic changes are fully discussed by Groover, Christie and Merritt.[3] Mühlmann[4] has described untoward effects in fatty tissue. The salivary glands and the mucous membrane of the mouth are

NOTE. Many of the data used in compiling this article were taken from Ewing's book entitled "Neoplastic Diseases."

very easily influenced. And yet more work must be done and many accurate observations recorded before we can set down definite figures indicating the tolerance of these normal tissues. It is true that figures representing the tolerance of various tissues have been published, but the very fact that different authors disagree on these tolerance doses argues against their accuracy.

Our knowledge of the sensitiveness of the many forms of malignant tissue is also rather chaotic. We know that malignant tumors arising in the testicle, larynx, uterine cervix and breast are much more sensitive than those arising in the prostate, rectum and stomach; but there is little written regarding the exact order of sensitiveness. Wood,[5] in an effort to illustrate the present uncertainty regarding tumor sensitiveness, sets down the widely different doses proposed by Bumm and Seitz and Wintz for the cure of the same tumor. Here again, accurate records augmented by good pathological reports where they are obtainable, will slowly build up a scientific system of therapy. It may be true that various histological types of cancer arising in the same location possess varying degrees of susceptibility to irradiation, according to the cell type. Many theories of this order have been backed by little or no recorded clinical evidence, and must therefore, stand as theories only.

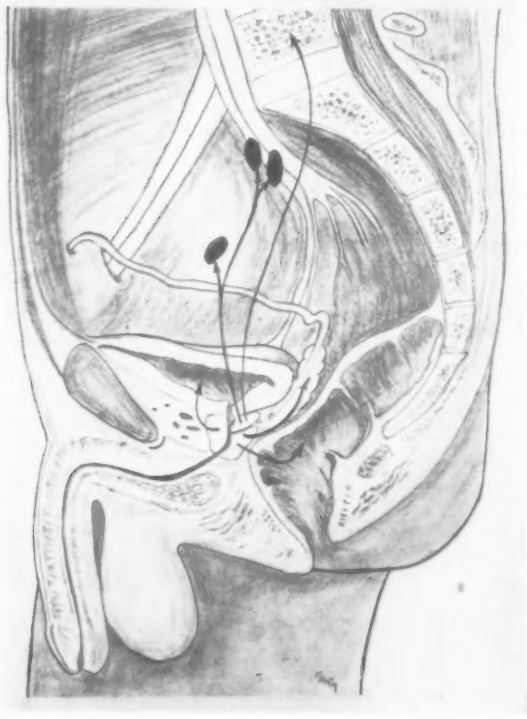

FIG. 1. Paths of metastasis within the pelvis secondary to carcinoma of the prostate.

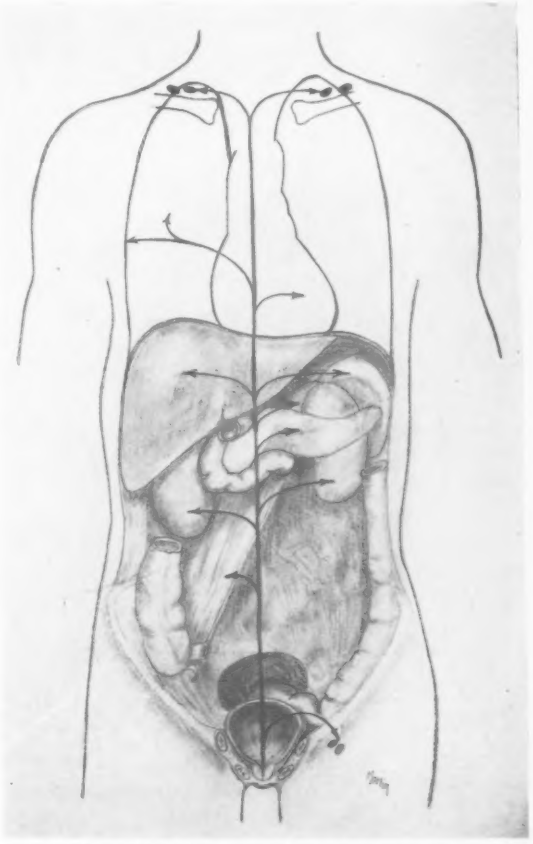

FIG. 2. Possible sites of wide-spread metastases in carcinoma of the prostate.

Although this biological data must be obtained in the future, there is much information now available relative to the distribution of cancer arising in the various well-known sites. Records written at the operating and autopsy tables indicate the relative malignancy of tumors and their most likely paths of extension. We have prepared a few charts illustrating the usual behavior of some of the more common neoplasms.

Figures 1 and 2 illustrate the mode of extension observed in carcinoma of the prostate. It is well to note that the pros-

tate is bounded behind by the rectum and above by the bladder, while the urethra runs through it. The dose delivered is, therefore, definitely limited by the mucous membranes of these structures, regardless of the efficiency of our apparatus. The available evidence indicates that carcinoma of the prostate is a very resistant tumor. Bumpus,[6] of the Mayo Clinic, reports only 3 patients alive three years, out of 217 receiving radium therapy. Deming,[7] who has had much experience with radium therapy in prostatic malignancy at the Johns Hopkins Hospital, insists on very heavy doses, and states: "Thus far we have no actual proof that radium has produced an actual cure for cancer of the prostate and seminal vesicles." However, he claims that 75 per cent of his patients receive symptomatic relief and 50 per cent of the cases suffering from pain in the back are made comfortable. Such benefit from irradiation makes the method well worth while, even though it may not produce an actual cure. Symptoms relieved are frequency, nycturia, hematuria, hesitancy, dribbling, small stream, complete retention, residual urine, pain in the back and extremities, and loss of weight.

In examining patients, it is well to remember that a malignant area may be concealed within a simple hypertrophy or may appear on top of a hypertrophy and give rise to a hard nodular gland. On the other hand, the malignant area may be so small that it gives practically no symptoms until the patient is riddled with metastases. The earlier paths of spread are shown in Figure 1. Extension upwards along the seminal vesicles is common and can usually be palpated by a finger in the rectum as a hard nodular mass. However, involvement of the bladder and rectum may occur. One of our cases showed actual obstruction from nodular masses surrounding, but not invading, the rectum. With the exception of the inguinal nodes none of the pelvic glands invaded through lymphatic distribution can be discovered by physical examination. Most radiologists are familiar with the bone metastases so frequently found accompanying a prostatic neoplasm. Since these lesions are common in the lumbar spine, hips and pelvis, films of these regions should be taken as a routine part of the examination. Figure 2 represents the widely separated sites that may become involved when extension gets well under way. In such cases the secondary lesions often bring the patient to a hospital without his ever realizing that the trouble started in the prostate. About two years ago an old man was brought to Baylor Hospital because of weakness, loss of weight, anemia, and vague digestive disturbances. The supraclavicular nodes were involved on both sides and a plate of the chest showed the mediastinal nodes enlarged. Irradiation was started with the belief that the patient had Hodgkin's disease. He grew worse continually and after several months, died. A tissue examination revealed a prostatic carcinoma. A careful examination in the beginning might have discovered the diagnosis at that time. An accurate diagnosis usually makes possible an intelligent prognosis and the institution of the most beneficial form of treatment.

Figure 3 represents the types of extension associated with carcinoma of the stomach. The surgeons are badly in need of help in the treatment of this malady. The better clinics report about 20 per cent of three-year cures where only selected cases are operated upon. A glance at the chart will explain this high mortality rate. The circle is drawn around the arrows representing early metastases. The liver and the nodes beneath it are invaded early. All radiologists are familiar with the fact that gastric malignancy usually gives definite symptoms only after it has become well advanced. Consequently, metastases are usually well under way before the patient seeks aid.

Gastric tumors are always in close proximity to many intestinal mucous surfaces, which limit the safe amount of irradiation that can be given. The scarcity of favorable reports in the literature leads us to the conclusion that gastric cancer must be very resistant to irradiation. Ernst[8] reports 3 cases which showed a gain in weight and a relief of pain for eight and nine months following copper-filtered *x*-ray therapy. Our own experience has not been so satisfactory. The distressing symp-

toms usually met with are cachexia, anemia, hemorrhage, pain and digestive disturbances. It is to be hoped that someone will publish a description of a large series of cases which have been followed up carefully after irradiation, in order that the degree of symptomatic relief obtainable may be ascertained. The marked treatment sickness which follows irradiation of the epigastrium makes the treatment of this region quite difficult. When metastases have reached the supraclavicular nodes, the brain, or the pelvic viscera, the problem of administering homogeneous irradiation becomes a most complex one. It would seem, therefore, that treatment of carcinoma of the stomach will not be likely to yield the most favorable results.

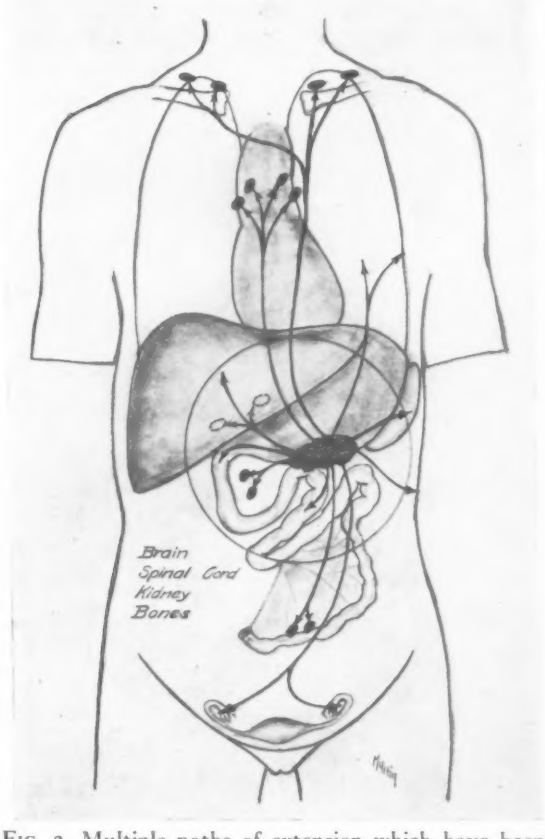

FIG. 3. Multiple paths of extension which have been observed with carcinoma of the stomach. The circle encloses earlier lesions which often appear before symptoms become prominent.

Figure 4 illustrates the extensions which usually accompany a carcinoma of the head of the pancreas. Malignancy of the tail and body does occur, but it is rare and its early detection is extremely difficult. The gall-bladder is shown markedly distended since the common duct is frequently occluded and a steadily progressive jaundice is one of the most suggestive symptoms. Epigastric pain is usually present and the patient shows a rapidly progressing cachexia. The tumor is almost completely surrounded by the duodenum and is covered over anteriorly by the stomach. Gastrointestinal mucosa, therefore, again limits the size of the safe dose. The literature offers little relative to the sensitiveness of cancer of the pancreas. Richards[9] reports 2 cases which showed increase in weight and relief of pain almost a year after copper-filtered irradiation. These results are encouraging. Since pancreatic metastases tend to remain within the abdomen and are usually situated within a relatively small area, the possibility of obtaining permanent results is much better than with gastric cancer where the extension is rapid and covers much territory.

FIG. 4. Carcinoma of the pancreas rarely spreads outside the abdomen and the metastases occupy a relatively small area.

The problem centers about the relative sensitiveness of pancreatic cancer and the intestinal mucosa. Since a dose too small to produce a cure will often cause a temporary remission in the growth of a resistant tumor, treatment for palliation only is worth while, even where the normal structures limit the most effective dosage.

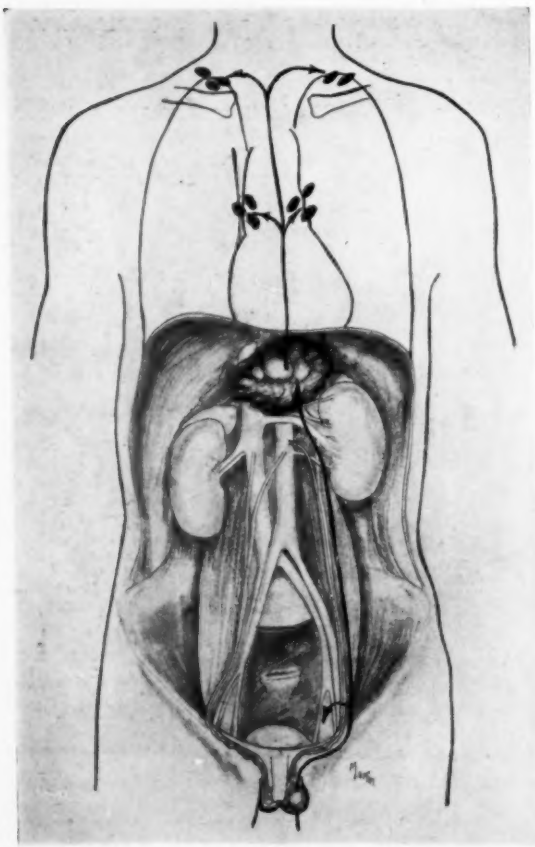

FIG. 5. Testicular tumors metastasize early and form rapidly growing abdominal tumors.

Cases of pancreatic malignancy are often operated on with a diagnosis of gall-stones. Such operations offer the radiologist an opportunity to discover the extent of metastasis; and he can plan his attack better after having been at the operating table. Surgeons usually do not trace out the various metastases, but a careful study of the conditions in the abdomen should be made if irradiation is to be resorted to. Where a cancer of the pancreas is discovered, a search should be made for enlarged glands beneath the liver and about the pancreas itself. The liver should be carefully examined, since the secondary nodules are sometimes quite small. The peritoneum and mesenteries should then be examined for nodules. It is especially important to determine the limit of downward extension if we are to treat all the diseased tissues.

The metastatic tendencies of malignant tumors of the testicle are illustrated in Figure 5. This drawing indicates only the paths of lymphatic distribution. Metastases following invasion of the iliac or spermatic veins may form new growths in the lungs, liver, brain, kidney and

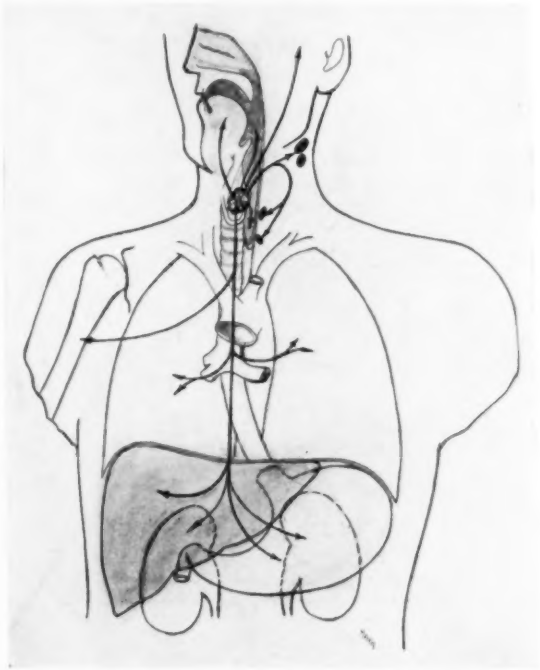

FIG. 6. Carcinoma of the larynx, when extrinsic in origin, may produce widely distributed secondary lesions, as shown by the arrows.

stomach. However, a large portion of the cases afflicted with this malady consult a physician because of a rapidly growing abdominal tumor, usually in the epigastrium. The primary growth in the testicle may have been completely overlooked. The lymphatics pass upward with the spermatic vessels and often the migrating cells pass rapidly up to the vicinity of the renal vessels before they begin to grow. They are occasionally halted further down and form tumors in the groin or iliac fossa. At a later stage mediastinal and

supraclavicular glands may be involved. The patients are usually young men who show a rapid loss of weight, fever, anemia and weakness as the disease advances. A great many of them have had one testicle removed shortly before the abdominal tumors appeared. These cases deserve a general examination, since it is of the greatest importance to attack the metastatic tumor. Fortunately, the cells of these tumors respond quite readily to irradiation. Bowing[10] reports prompt disappearance of the metastases in many of his cases treated with both radium and roentgen rays. Good results are usually obtained if the disease has not progressed too far. The tumors grow rapidly and metastases form very early. Surgical removal of the testicle often fails to cure the patient and should always be accompanied by irradiation applied to the epigastrium and along the whole length of the spermatic vessels. We have found no reliable data relative to three- or five-year cures in such conditions. Let us hope that accurate records of progress are being kept in some of the laboratories where such cases are under treatment.

The situation encountered in carcinoma of the larnyx is roughly represented in Figure 6. The points of origin of tumors in this region influence their clinical course. When the origin is intrinsic, that is, in or about the vocal cords, the tumor usually grows very slowly, is accompanied by considerable ulceration and secondary infection, and gradually invades the neighboring tissues, causing death by dysphagia, hemorrhage, suppuration and a terminal infection. When the origin is extrinsic, metastases form fairly early in the glands of the neck, both superficial and deep. Direct extension occurs in the tongue, pharynx and esophagus. The primary growth shows a marked tendency toward ulceration followed by suppuration. Late metastases may be found in the brain, chest and abdomen as indicated in the drawing. Cancer of the larynx is advantageously located for treatment, since it is near the surface and is accessible from several angles. The tracheal mucosa and the salivary glands are quite sensitive, but we at present have no accurate data concerning their relative sensitiveness as compared with that of laryngeal carcinoma. It has been shown however, that this type of growth often responds readily to irradiation therapy. The case reports published by Quick and Johnson,[11] Freer[12] and Pfahler[13] are most convincing.

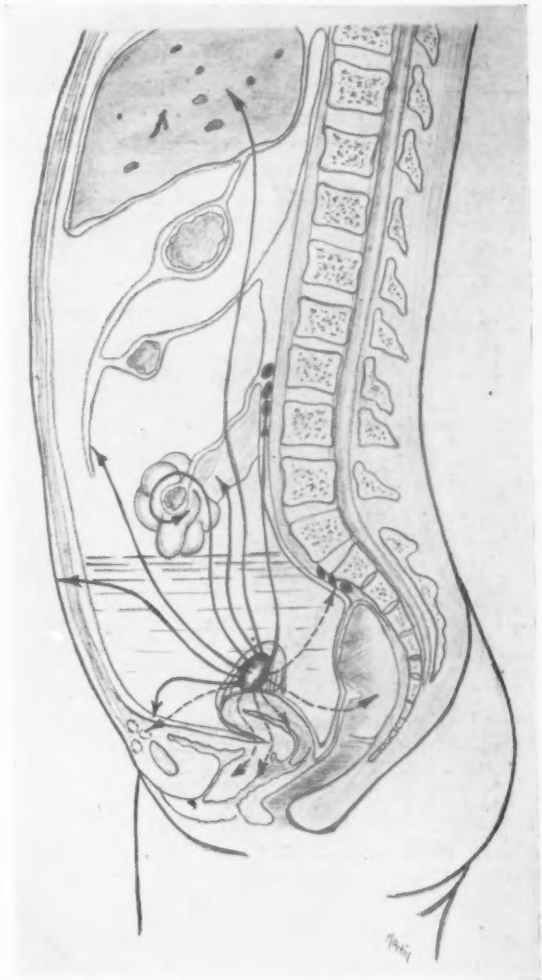

FIG. 7. The solid arrows represent the lines of spread observed with tumors of the ovary. The broken lines represent the paths of metastasis from intraligamentary tumors.

It is a puzzling fact that a certain number of the cases treated by these authors showed no improvement, while others cleared up rapidly. An investigation of the causes of these differences would be most interesting. One of our own cases showing almost complete occlusion of the pharynx and large cervical glands has remained free of visible pathology for eight months follow-

ing copper-filtered irradiation. Good results can, therefore, be obtained with a number of these patients if they consult a radiologist before distant metastases have appeared.

The lines of extension commonly observed with malignant tumors of the ovary are portrayed in Figure 7. These tumors may be either cystic or solid, and the majority of them grow slowly and show a low grade of malignancy. The first symptoms are often caused by the metastases which commonly appear in the peritoneum, particularly the mesenteries and omentum, shows a lateral view of the abdomen of a woman who had developed many large omental masses and adhesions and came to the hospital because of vague digestive disturbances associated with ascites. Needless to say, it is quite important to obtain a full report regarding the extent of metastases from the operating surgeons when a malignant ovary is removed. The outlook in cases showing a few peritoneal implantations in the pelvis is far superior to that in cases showing general abdominal extension.

FIG. 8.—Lateral view of the abdomen following the removal of 4 qts. of fluid and the introduction of carbon dioxide gas in an advanced case of carcinoma of the ovary with multiple abdominal masses and adhesions.

and may produce interference with peristalsis and actual obstruction. Ascites is likely to be present and adhesions may be plentiful. In advanced cases the liver and retroperitoneal glands are invaded and rarely subcutaneous nodules and bone metastases occur. Two cases have been referred to us which were operated on for intestinal obstruction. The cause of the obstruction was revealed by the pathologist who examined the resected specimens. The paths of spread for intraligamentary tumors are usually downward rather than upward, as indicated by the broken lines in the drawing. Roentgenograms of the abdomen made following the removal of fluid and the production of pneumoperitoneum have helped to make a diagnosis in well-advanced cases. Figure 8

The determination of the sensitiveness of ovarian tumors to irradiation is difficult. Most of the cases are treated after the primary growth has been removed surgically, and it is a well-known fact that peritoneal implantations often show spontaneous retrogression where no treatment of any kind is given following operation. It is not fair, therefore, to give all the credit for clinical improvement to irradiation. Schaefer[14] reports some excellent results in cases irradiated following radical surgery, although he had a number of failures. Belot[15] claims to have caused a disappearance of ascites and general improvement in a case with peritoneal metastases treated following operation. This evidence justifies the treatment of such patients, although the dosage must be

regulated so as to safeguard the intestinal tract.

Figure 9 represents the paths of extension ordinarily observed with carcinoma of the fundus of the uterus. This lesion usually appears at or after the menopause, and the first sign is a discharge which later becomes bloody. Pain is a very late symptom. The discharge is likely to appear while the tumor is localized within the thick walls of the uterus, and consequently surgical removal is the treatment of choice in the earlier cases. The network of lymphatics which surrounds the tubes and ovaries is often invaded; it is therefore wise to do a total hysterectomy, if operation is decided upon. The symptoms of carcinoma of the fundus are identical with those caused by a number of benign lesions which may occur in the uterus, and a diagnostic curettage is the most essential step in making a diagnosis. One of the *x*-ray tables in our laboratory is made with a drop leaf and detachable stirrups, and an electrical sterilizer is placed near by. A diagnostic curettage can be done without materially disturbing the equipment of the *x*-ray room. All pelvic cases are examined on this table before and after treatment. When the lumbar, iliac or inguinal nodes have become involved, irradiation must be resorted to. Unfortunately, only the inguinal nodes are palpable from the outside, but it seems rational to cover the region occupied by the iliac and lower lumbar nodes in administering treatment, since they may also be involved. Clark[16] reports 12 cases alive from three to six years following the use of radium. Although it is not so stated, it is intimated that these were early cases. We have at our disposal no records indicating the sensitiveness of the cells making up the metastatic deposits in the nodes. One of our own cases developed a recurrence in the abdominal wall following operation. A very large dose of copper filtered *x*-rays was administered to this nodule which was just below the skin. The dose was large enough to cause a bloody diarrhea. The nodule completely disappeared, but returned in six months and began to grow rapidly. The same dose

FIG. 9. Carcinoma of the uterus extends beyond the uterine walls at a late stage in the disease along the paths indicated by the arrows.

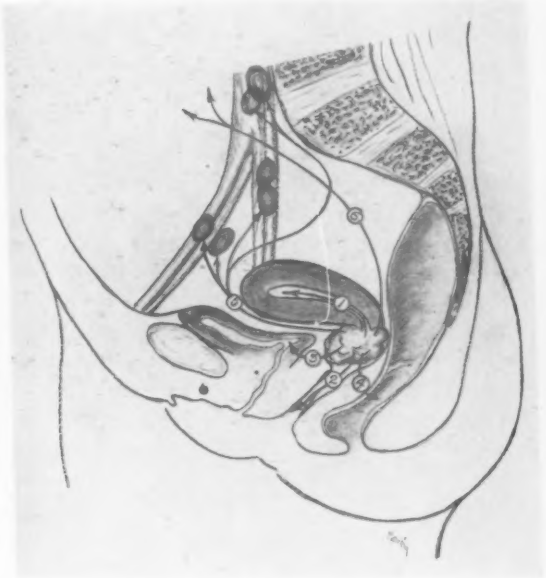

FIG. 10. Metastases from carcinoma of the cervix are usually limited to the soft tissues of the pelvis. Arrow No. 6 represents extension into the abdomen, which is a rare occurrence.

was repeated with the same intestinal effect and the nodule again disappeared, only to reappear in about six months. Conclusions should not be drawn from one case, but we are inclined to believe that the cells of these tumors are quite resistant so far as complete extermination is concerned.

The mode of spread accompanying carcinoma of the cervix is indicated in Figures 10 and 11. Almost everyone is familiar with the triad of symptoms (discharge, hemorrhage and pain) which is so characteristic of this affliction. The diagnosis of the primary lesion is usually easy where facilities for doing a routine pelvic examination are available. One of the most important procedures is a rectal examination. This is not done in an effort to examine the rectum itself, so much as to determine the degree of extension of indurated tissue out along the broad ligaments. Such extension is almost invariably present except in very early cases and its presence or absence plays an important rôle in the prognosis as well as the treatment. Should this induration be discovered when the cervix looks normal, the upper cervical canal should be examined with great care for the type of cancer that begins above the field of vision. On two occasions such cases were referred to us with a diagnosis of fibroids of the uterus by clinicians who had been misled by the normal picture seen through the speculum. A cystoscopic examination will determine the condition of the posterior bladder wall, which often has an appearance suggesting a group of crowded vesicles when actual invasion has occurred. Pain has, in our experience, many times been secondary to stricture of the ureter (Fig. 11) and in such cases a genito-urinary consultant is asked to catheterize the ureter on the affected side, and a pyelogram is made. One is struck at once in studying advanced and recurrent cases with the frequency with which the chief complaint is pain in one hip and one side of the pelvis referred down to the groin and inner side of the thigh and up to the costovertebral angle. A high fever coming on top of such symptoms usually indicates the presence of a pyonephrosis. Figure 12 shows a dilated ureter and kidney pelvis which were produced by such a malignant stricture. Irradiation in this case gave complete relief of pain for a period of a year. However, such treatment has in our hands often failed to relieve these

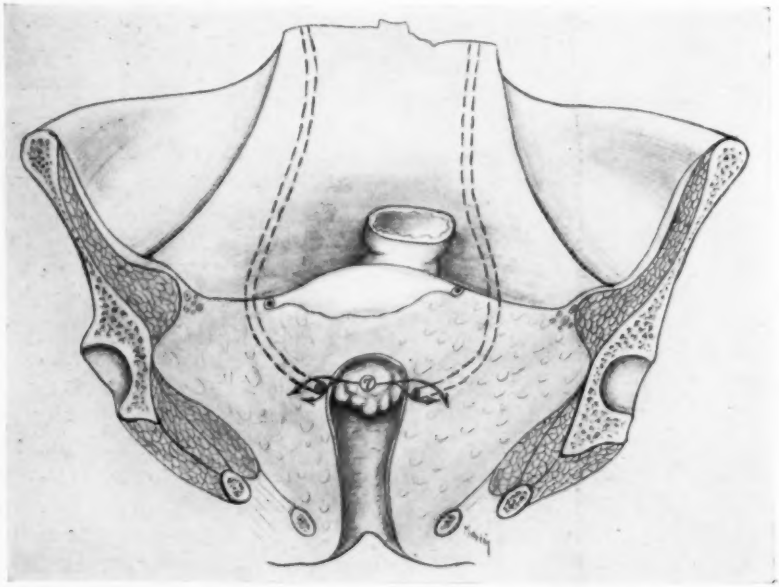

FIG. 11. Lateral extensions into the parametrium with occlusion of the ureters usually produce the fatal outcome in carcinoma of the cervix.

strictures. When both ureters are stenosed death is imminent. Ewing[17] states: "The natural termination of most cases of uterine cancer is through uremia from occlusion of the ureters." Fever is as likely to be due to a cystitis or pyelitis as an infection in the growth itself. Such an infection should be treated medically before irradiation is begun. Fistulae opening either into the rectum or the bladder may often be closed or partially closed by applying radium to the edge of the opening in quantities sufficient to cause marked contraction. The severe skin irritation about the vulva accompanying a fecal fistula has healed when kept continuously covered with a coating of zinc oxide

FIG. 12. Pyelogram illustrating a hydronephrosis caused by a stricture of the ureter secondary to carcinoma of the cervix. The symptoms were typical of stricture of the ureter.

ointment. Arrow 6 in Figure 10 represents extension up into the abdomen, but this type of extension is rarely encountered. It is for this reason that carcinoma of the cervix and its compactly arranged metastases are so effectively rayed. The deep pelvic glands are invaded late in the disease, but their enlargement cannot be detected from the outside of the body. When large doses are applied it should be remembered that the cervix is bounded in front by the bladder and behind by the rectum.

The proof in the literature of the sensitiveness of carcinoma of the cervix is too extensive to be doubted and no attempt will be made to set down the many references which describe excellent results. It is an established fact that many early

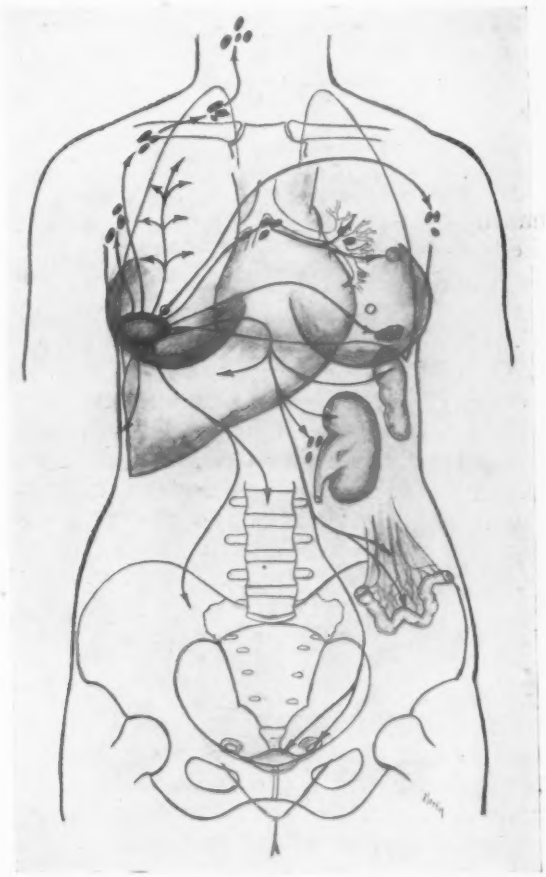

FIG. 13. The complicated metastatic possibilities in carcinoma of the breast.

cases have been cured and many advanced ones relieved of symptoms. It is somewhat discouraging to note that Seitz[18] was unable to increase his percentage of five-year cures when deep *x*-ray therapy was added to the radium therapy already in use. Involvement of the bladder, rectum, vagina or ureters makes the prognosis poor, and the presence of such involvement should be known before treatment is begun.

The chart shown in Figure 13 represents the very complex situation encountered

in cancer of the breast. It would be well for the surgeon to have this chart in mind when he is contemplating the removal of a breast for carcinoma, since many of these metastases occur early and are not touched by the most radical operation. This statement is well borne out by a table of statistics published by Sistrunk and McCarty,[19] of the Mayo Clinic. Two hundred eighteen cases operated upon for cancer of the breast were followed for five to eight years. Only 63.9 per cent of those showing no glandular involvement and 18.9 per cent of those showing glandular involvement were alive at the end of that period. In other words, 36.1 per cent of the cases having no glands in the axilla or neck died of metastases, and those cases that did have glands palpable had only one chance in five of being cured by a radical amputation. Obviously, the surgeon needs help. A careful physical examination should precede any form of treatment. Both axillae, both sides of the neck, both breasts and the subcutaneous tissues in general should be gone over with the fingers. The liver edge should be palpated and the abdomen examined for masses. Films of the chest, spine and pelvis should then be made, regardless of the symptoms. Films of the chest are of the greatest importance and should be repeated at regular intervals following treatment, since lung lesions often come on insidiously and cannot be detected with the stethoscope until they reach a considerable size. The various types of pulmonary lesions are well described by Carman.[20] Several cases have been referred to us following operation with definite lung involvement. These patients might have been saved a major operation if a radiologist had been called in consultation when the preliminary examinations were made. During the past three years we have treated our postoperative cases by covering the lymphatic channels over the chest as thoroughly as possible. Very few of these cases have developed pulmonary metastases. The majority of those that did not do well died with extreme pain in the lower back and hips, often in the absence of demonstrable bone lesions. We have assumed that the pain was due to the presence of enlarged retroperitoneal glands. Be that as it may, it seems probable that abdominal metastases were present at the time that treatment was started. The problem of applying homogeneous irradiation to such a widespread distribution of diseased tissue is not an easy one. We have been considering the advisability of beginning treatment over the lower spine and working upward, since the terminal lesions are so often in the lower portion of the body. There is no method available for the detection of most of the subdiaphragmatic secondary lesions and it is probably best to assume that they are always present.

Proof of the sensitiveness of the cells of breast cancer to irradiation is abundant and need not be established here. Numerous reports of the retrogression of palpable glands are also available. That deep-seated lesions may also be favorably influenced is illustrated by the roentgenograms of the chest shown in Figures 14 and 15. On Mar. 2, 1921, the patient underwent a radical removal of the left breast, and *x*-ray treatment was advised. The tumor was found to be an adenocarcinoma, but no histological evidence of malignancy could be made out in the axillary glands. The chest was clear at the time of the operation. Soon afterward a hard subcutaneous mass was found in the epigastrium and was rayed vigorously. The patient did well until Mar. 8, 1922, when she returned because of pain in the posterior portion of the right chest. The roentgenogram shown in Figure 14 was made at that time. The circular plaque seen at the right base is characteristic of malignancy and appeared to be attached to the diaphragm. The anterior posterior diameter of the chest measured 7 in. We administered 720 ma. min. to an area 20 cm. square laid out on the back of the right chest so that it was centered over the lesion shown in the film. The dose was given with 6 ma. flowing at a sphere-gap reading of 140 kv., a target-skin distance of 12 in., and a filter of ½ mm. Cu. and 1 mm. Al. We gave 360 ma. min. over the anterior chest wall using an area 15 cm. square. On Oct. 7, 1922, she returned, showing no loss of weight or

strength. A film of the chest showed a retrogression of the plaque shown in Figure 14. She still complained of pain. We gave 360 ma. min. over the back over a 20 cm. square, but the patient refused further treatment because of a severe treatment sickness. On Mar. 17, 1923, she felt better and had still lost no weight. Figure 15 shows the chest as it appeared at that time. The nodule had almost completely disappeared. A year and four months have elapsed since the first treatment was given and the patient states in a recent letter that she feels well and is now free of pain. This case illustrates the importance of being constantly on the alert for new metastases. A repeated careful physical examination is by no means the least important procedure coupled with deep therapy.

This brief paper illustrates a few of the problems in radiotherapy outside the field of physics. Needless to say there are numerous types of malignant tumors that we have not touched upon. An article dealing with all the known varieties would approach a book in size.

SUMMARY

The deep therapist should know something of the sensitiveness of the normal structures, the sensitiveness of neoplastic cells and the usual clinical progress of the various types of neoplasms, as well as the pure physics of depth-dose determination. Carefully written records containing repeated physical examinations will eventually establish the true value of our recent progress in *x*-ray physics as applied to the patient. The radiologist who can make an accurate diagnosis and give a reliable prognosis will soon acquire a place of dignity among his fellow-practitioners of medicine.

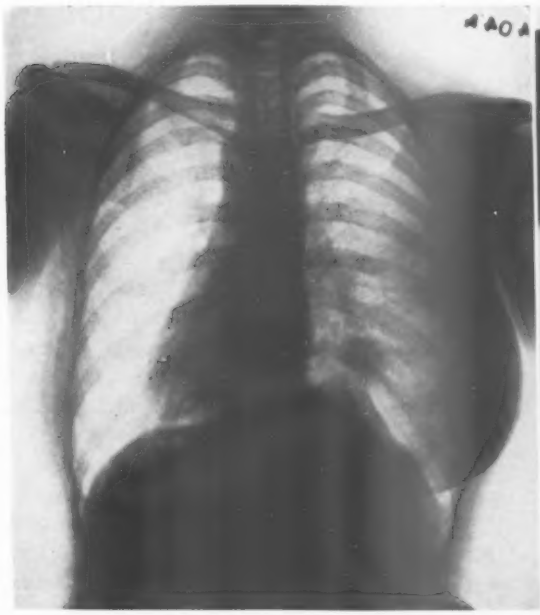

FIG. 14. An early metastatic nodule within the base of the right lung secondary to carcinoma of the left breast.

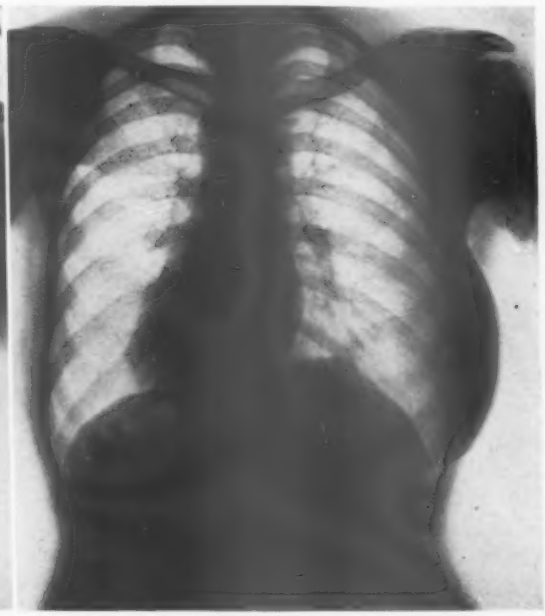

FIG. 15. A film of the chest shown in Figure 14 one year later. This result was obtained with intensive irradiation.

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BIOLOGICAL REACTION OF X-RAYS: THE INFLUENCE OF X-RAY TREATMENT ON THE COMPLEMENT CONTENT OF THE BLOOD OF CANCER PATIENTS

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AMONG those constituents of the blood which vary in normal individuals within only very narrow limits is the complement. Mandelbaum[1] in 1916 stated that the complement content of the blood, if examined immediately, is constant not only for normal individuals, but also in a variety of diseases. This data for normal individuals was substantiated by Cori and Radnitz[2] in 1920, but could not always be confirmed in the case of diseased individuals.

No variation in the complement content of the blood of normal persons was observed even when examined during successive days or weeks. In disease, however, variations of the complement contents from its normal value may occur. Thus during the febrile period of various infections the complement is very often increased, returning again to normal at the end of the fever period.

This paper shows that patients under *x*-ray therapy may exhibit variations of the complement. These variations rapidly adjust themselves to normal after the *x*-ray treatment. Our data show that there are mechanisms in the body which attempt always to keep the complement at the same level. This fact is particularly brought out by Schütze and Scheller[1] who have proved that the complement of rabbits is restored in two to four hours after it has been completely used up by the injection of washed sheep corpuscles.

In a previous investigation[2] it was found that the complement titre of patients subjected to *x*-ray treatment is changed from its normal value. These experiments were repeated on a larger scale to see if there was any relationship between the amount of radiation received by the body and the variation of the complement.

EXPERIMENTS

The titration of the complement was as follows: 3–4 c.c. of blood was drawn from the cubital vein and centrifuged as soon as the blood was clotted. The clear serum was quickly worked up so that forty minutes after the blood was taken the system could be placed in the incubator. For the dilution of the serum the following technique was used: 0.5 and 0.4 c.c. of the serum was diluted to 1 c.c. with normal saline, 0.5 c.c. of these mixtures were transferred to other tubes containing 0.5 c.c. salt solution and the process con-

[1] Mandelbaum. *Münch. med. Wchnschr.*, 1916, p. 1039.
[2] Cori and Radnitz. *Ztschr. f. Immunitätsforch.*, 1920, xxix, 445.

[1] Schütze and Scheller. *Ztschr. f. Hyg., u. Infections-krankh.*, 1901, xxxvi, 459.

tinued as often as desired. In this manner different dilutions of serum were obtained, each subsequent dilution being exactly half of the preceding one. Each tube was made up to 1 c.c. by the addition of 0.5 c.c. normal saline. One c.c. of sensitized corpuscles was then added and each tube thoroughly mixed and incubated for one hour at 37° when the final reading was taken. The first tube that showed complete hemolysis and no trace of turbidity on shaking was chosen as the dilution indicating the titre of the serum. The dilution of serum in the tables is expressed as c.c. of serum present in each tube. The following dilutions were employed: 0.2, 0.125, 0.1, 0.075,[1] 0.06, 0.05, 0.03, 0.025, 0.015.

The sheep corpuscles were sensitized as follows: equal parts of 2.5 per cent corpuscles and amboceptor were mixed together as quickly and thoroughly as possible. The amboceptor obtained from the Lederle Antitoxin Company was used in a concentration three-fold the strength necessary for complete hemolysis.

In connection with this investigation it was of greater importance to calculate the entire *x*-ray dose received by the body than to record the skin dose or the tumor dose, since changes in the complement are systemic effects. For the calculation of this body dose a certain unit "Ax" was used, the definition of which will be given by Dr. Stenström in another paper.

TABLE I

THE COMPLEMENT CONTENT OF THE BLOOD OF NORMAL PERSONS

Cases	Date	Complement
1	10/18/22	.05
	4/17/23	.05
2	10/18/22	.06
	4/17/22	.05
3	10/18/22	.05
	10/18/22	.03
	4/17/22	.05
4	10/18/22	.05
5	10/18/22	.05
6	10/18/22	.05
7	10/18/22	.05

This table shows that there is no appreciable variation in the complement content of normal individuals. The normal value for complement is 0.06–0.05.

[1] The tube containing 0.075 c.c. of serum was prepared from the dilution 0.25, the latter being omitted.

TABLE II

COMPLEMENT CONTENT OF THE BLOOD OF TUMOR PATIENT

Cases	Complement
2	.1
3	.075
12	.06
37	.05
13	.03
8	.025
2	.015

The data indicates that 64 per cent of the patients examined were within the normal complement limits, while 30 per cent were above and 6 per cent below the average value. All these cases with the exception of 2 had a negative Wassermann. The influence of radiation on the complement contents of the blood of tumor patients is shown in Tables III, IV and V.

These tables show the following facts:

1. Patients under *x*-ray treatment may undergo changes in their complement values. These variations of complement content do not seem to bear any close relationship to the amount of radiation received by the body, since patients with the same type of lesion and same quantity of radiation may show an increase or decrease of complement. This behavior reveals great individual differences of patients in their response to radiation. This is in contrast to the more uniform sensitiveness of the skin toward *x*-rays as measured by the constancy of the erythema dose.

2. Table IV, in which very small radiation was employed, tends to show that no change in complement occurs below 150 Ax. Above this quantity of radiation changes of complement are likely to take place. However, no general rule can be made, since it will be seen (Table III) that even with very high radiation (3,590 Ax) no fluctuation of complement will occur.

3. It is interesting to note that a large percentage of those patients in whom a pronounced drop of complement took place after radiation had already died when this work was completed. This observation may be of prognostic value for determining whether it is safe to continue with *x*-ray treatment. Thus it may be used as a measure of the amount

TABLE III

EFFECT OF HEAVY RADIATION ON THE COMPLEMENT CONTENT OF THE BLOOD OF CARCINOMA PATIENTS

Carcinoma of the Cervix

	File Number	Lesion	Complement Before		Body Dose		Complement After		Remarks
			Date	Value	Date	Ax	Date	Value	
1	7415	Group 4	2/27/22	.06	2/28/22	1040	3/1/22	.2	Died
2	7473	.....	11/23/22	.05	11/27/22	1110	11/27/22	.05	
3	7744	Group 3	1/11/23	.05	1/11/23	1490	1/12/23	.05	
4	6969	Group 4	3/28/22	.03	3/30/22	1630	3/31/22	.05	
5	7748	Group 2	10/24/22	.05	10/24/22	1820	10/24/22	.05	
6	7872	Group 3	2/19/23	.025	2/19–20/23	1950	2/21/23	.03	
7	7754	Group 4	10/10/22	.015	11/14–15/22	2250	11/16/22	.075	
8	7646	Group 4	3/ 7/23	.05	3/ 8/23	2510	3/ 9/23	.06	
9	7871	Group 4	2/22/23	.05	2/22–23/23	2730	2/23/23	.05	No history
10	7653	Group 3	11/28/22	.05	11/28/22	2970	11/29/22	.05	No history
11	7869	Group 3	2/19/23	.05	2/20–21/23	3070	2/21/23	.05	Died April, 1923
12	7665	Group 3	4/ 4/23	.05	4/ 6/23	3590	4/ 7/23	.05	
13	7830	Group 4	2/27/23	.05	2/27/23	3540	2/28/23	.05	
14	7094	Group 3	1/ 9/23	.05	1/ 9/23	3670	1/11/23	.025	
							1/16/23	.05	
15	6156	Group 4	4/ 7/22	.05	4/ 6/22	3710	4/ 6/22	.125	Died July, 1922
							4/11/22	.05	
16	7887	Group 4	1/23/23	.05	1/23/23	3960	1/23/23	.03	
17	7778	Group 3	11/22/22	.05	11/22/22	4080	11/23/22	.025	
18	7875	Group 2	2/21/23	.05	2/21/23	4590	2/22/23	.025	
			Carcinoma of the Rectum						
1	7737	Group 3	10/27/22	.025	11/24/22	1780	11/25/22	.05	
2	7374	Group 4	4/19/22	.05	4/20/22	1780	4/21/22	.2	Died Oct., 1922
							4/27/22	.05	
3	7398	.....	3/21/22	.03	3/21/22	1680	3/22/22	.2	No history
4	7199	.....	4/25/22	.06	4/26/22	1530	4/26/23	.1	Died Feb., 1923
							5/ 1/23	.05	
			Hypernephroma Right Kidney						
1	7393	.....	3/28/22	.05	3/30/22	1460	3/31/22	.125	
2	7863	.....	2/ 8/22	.03	2/ 8/22	1300	2/ 8/22	.03	
			Carcinoma of the Breast						
1	7350	Group 3	3/19/22	.05	3/19–20/23	960	3/20/23	.03	
2	7703	Group 3	3/ 8/23	.06	3/ 9/23	1350	3/ 9/23	.06	
3	7292	Group 4	12/14/22	.1	12/14/22	1370	12/16/22	.03	
							12/20/22	.1	Died June, 1922
4	7041	Group 4	3/19/22	.06	3/20/22	1760	3/20/22	.025	
							4/12/22	.05	
5	7347	.....	3/ 2/23	.03	3/ 2/23	2280	3/ 2/23	.025	
6	7315	.....	3/24/22	.05	3/29/22	3080	3/ 3/22	.05	
7	6615	Group 4	3/27/22	.05	3/27/22	3140	3/27/22	.05	
8	6681	Group 4	3/16/22	.075	3/ 6/22	3230	3/ 7/22	.1	
9	6403	.....	1/23/23	.06	1/24/23	3710	1/24/23	.03	
							2/ 1/23	.06	
			Carcinoma of the Esophagus						
1	7740	.....	11/28/23	.05	11/28/23	1320	11/29/23	.03	No history
			Carcinoma of the Bladder						
1	7889	.....	3/ 6/23	.03	3/ 7/23	1900	3/ 7/23	.05	
			Sarcoma of the Bone						
1	7677	Group 3	11/25/22	.06	11/27/22	1360	11/27/22	.03	Died May, 1923
			11/31/23	.06	2/ 1/23	1480	2/ 1/23	.03	

TABLE IV

EFFECT OF LIGHT RADIATION ON THE COMPLEMENT CONTENT OF THE BLOOD OF CARCINOMA PATIENTS

	File Number	Lesion	Complement		Body Dose		Complement	
			Date	Value	Date	Ax	Date	Value
1	7431	Lip	5/12/22	.025	5/12/22	*	5/12/22	.03
2	6319	Cheek	5/18/22	.03	5/19/22	*	5/19/22	.03
3	7529	Lip	5/16/22	.025	5/16/22	*	5/16/22	.025
4	7490	Lip	5/24/23	.05	5/24/23	*	5/24/23	.05
5	7509	Lip	5/19/22	.05	5/19/22	*	5/19/22	.05
6	6750	Breast	6/ 5/22	.025	6/ 7/22	*	6/ 7/22	.025
7	7718	Cervix	3/22/22	.05	4/ 8/22	130	4/ 8/22	.03
8	6930	Lip	5/13/22	.025	5/13/22	150	5/13/22	.025
9	6737	Lip	5/28/22	.05	5/25/22	170	5/25/22	.05
10	7467	Arm	3/30/22	.06	3/30/22	210	3/31/22	.03
11	5912	Larynx	1/11/22	.05	1/11/22	400	1/12/22	.05
12	6726	Cheek	5/10/23	.025	5/13/23	430	5/13/23	.015
13	7683	Lymph-nodes	11/23/22	.06	11/23/22	460	11/23/22	.075
14	7470	Jaw	4/ 3/22	.075	4/ 3/22	480	4/ 3/22	.03
..	....	.....	.....	....	.....	...	4/ 4/22	.075
..	....	.....	.....	....	.....	...	4/ 5/22	.075
15	7411	Thorax	2/25/22	.1	2/27/22	570	2/28/22	.075
16	7683	Lymph-node	11/28/22	.05	11/28/22	720	11/28/22	.05
17	7260	Ear	3/13/22	.075	3/14/22	800	3/14/22	.075

*Four-minute treatment.

TABLE V

EFFECT OF DIVIDED X-RAY DOSES ON THE COMPLEMENT CONTENT OF THE BLOOD OF CARCINOMA PATIENTS

Number	Lesion	Complement		Body Dose		Complement		Remarks
		Date	Value	Date	Ax	Date	Value	
7879	Breast	2/27/23	.05	3/ 6/23	790			
	Group 1	3/ 1/23	.05	3/ 7/23	790	3/ 7/23	.025	
		3/ 3/23	.05	3/ 8/23	790			
				3/ 9/23	790	3/ 9/23	.025	
						3/12/23	.03	
						4/ 9/23	.05	
7925	Breast	3/26/23	.05					
	Group 3	4/ 2/23	.05	4/ 2/23	1600			
				4/ 3/23	1600	4/ 3/23	.075	
				4/ 4/23	1600			
				4/ 5/23	1600			
				4/ 6/23	1600			
				4/ 7/23	1600	4/ 7/23	.075	
						4/ 9/23	.06	
						4/30/23	.05	
7918	Femur	3/19/23	.03					
		3/20/23	.03					
				3/21/23	480			
				3/22/23	480	3/22/23	.05	
				3/23/23	480	3/23/23	.06	
						3/24/23	.05	

of radiation tolerated by the individual. To establish finally the practical application of this observation it would be necessary to evaluate the complement of a large series and variety of cases.

In order to see if these variations of the complement were due to the direct action of the *x*-rays on the blood, the following test-tube experiments were performed. Defibrinated blood or serum of patients which showed an increase of their complaint on radiation was placed in narrow test-tubes of equal diameter and subjected in a thin layer to radiation. As soon as radiation was completed the tubes were placed on ice and the titre determined as quickly as possible. Control tubes were treated in a similar manner with the exception that they received no radiation. In these experiments an increase of complement was never observed. On the contrary a decrease took place after about eight to ten minutes' radiation with 2.5 mm. Al., 141 kv., 5 ma. and 30 cm. distance. These facts indicate that the increase of complement observed after the *x*-ray treatment of certain patients is due to factors other than the influence of radiation on the blood itself. Since in spite of the destruction of the complement of *x*-rays patients after radiation often show no change or even an increase, one must assume that new complement is being liberated into the blood stream. In those patients showing a diminution of the complement the regenerative process is, or has been, apparently delayed. That this is the case is shown in Table III by the fact that the complement eventually returns to its original value. The rate of regulation of the complement is best seen in Table V, where divided *x*-ray doses were employed.

Thus it will be seen that it takes several days for the complement to return to its original value, whether it has been increased or decreased by the *x*-ray treatment.

CONCLUSIONS

1. The complement content of the blood of normal individuals varies within very narrow limits (0.06–0.05).

2. *X*-ray treatment may cause an increase or decrease of the complement.

3. These changes in the complement are not closely related to the total amount of radiation received by the body, but seem to depend upon the individual difference of the patients treated.

4. The complement always returns gradually to its original value after the *x*-ray treatment has been discontinued.

5. A decrease of complement is always obtained when blood or serum is radiated *in vitro*. This fact indicates that the increase of complement observed after the *x*-ray treatment of certain patients is due to factors other than the influence of radiation on the blood itself.

6. A pronounced drop of complement after *x*-ray treatment seems to be of prognostic value, since the majority of those patients who showed this reaction had already died when this work was completed.

We wish to thank Dr. B. F. Schreiner for the privilege of examining the charts, and Miss Cora Geisler who assisted in some of the determinations.

TUMORS OF THE PITUITARY GLAND*

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THE marked interest in tumors of the pituitary gland and its secretory disturbances within the past few years has been due not only to the intensive study of endocrinology and the internal secretions by the medical profession as a whole, but in a larger measure to the greater accuracy with which an early diagnosis of hypophysial lesions can be made. Since the results obtained by operative procedures for pituitary tumors have been so encouraging in the early cases, the operation is no longer dreaded as formerly, and the risk is no longer as great on account of the advance and development of improved surgical technique.

An increasing number of these cases is daily being sent to the roentgenologist for study of the appearance of the sella turcica and skull. The roentgenologist, if he be in the truest sense of the word a consultant, daily reminding himself above all else that he is a physician practicing roentgenology rather than a technician, should be familiar with some of the evidences of the symptomatology, clinical history and physical findings in disturbances of the pituitary gland.

In arriving at an early diagnosis of pituitary tumors, there should be the closest correlation of the findings of the ophthalmologist, neurologist, surgeon and roentgenologist. To wait until marked optic atrophy has occurred before making a diagnosis leaves no hope of restoring the patient's vision; for then an operation will give no relief. The importance of making an early diagnosis cannot be too strongly emphasized.

Most of these patients begin to notice failing vision and headaches, and it is these symptoms that send them to the physician. The lowered visual acuity is not relieved by glasses. The headaches are usually bitemporal and worse at night. All or a part of the following symptoms accompany the ocular changes: headache, accession of bodily weight, increase in the size of the hands and feet, spacing of the teeth in the inferior maxilla, sexual impotence, drowsiness and inability to concentrate on mental work.

Since in many cases there is an absence of constitutional disorders and negative findings of the central nervous system, the ocular changes and roentgen-ray appearance of the sella offer the best means of making an early diagnosis.

The symptoms then, in pituitary lesions may be classified as those due to: (1) Secretory derangements, hyper- or hypo-pituitarism, (2) those resulting from extension or involvement of the surrounding cerebral structures, (3) headache resulting from intracranial pressure, (4) those due to involvement of the optic chiasma and tract.

With the varying symptomatology of the secretory disturbances of the gland we shall not deal. In fact it is extremely doubtful if surgery should ever be advocated for anything other than failing vision, or relief of intracranial pressure with accompanying headaches.

The ocular findings depend upon the size and position of the tumor; but the characteristics most often noted are lowered visual acuity, a progressive narrowing of the visual field, showing either a bitemporal or homonymous hemianopsia, with at times absence of light perception in one eye and temporal defects in the other eye. Near vision as well as distant vision is usually affected. In all stages the loss of color perception is usually in advance of that for form and the first perimetric indication of the process is shown by a temporal form field and a corresponding quadrantal defect in the color peripheries.

Benedict of the Mayo Clinic reports a peculiar pallor of the nerve head without shrinkage, which is seen so often that it is almost diagnostic. This pallor is not due to atrophy of the optic nerve, unless the vision has been entirely destroyed. The nerve substance itself is pale, but otherwise not noticeably changed. This pallor may appear in about four months after

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the onset of visual disturbances. If of longer duration in showing up, there most probably is a slow-growing tumor. Early optic atrophy indicates rapid pressure changes and is usually due to malignant tumors or cysts. Benedict, in reviewing 32 cases, reports lowered visual acuity of one or both eyes in every case. The onset of visual disturbances most frequently is gradual. He mentions one case of pituitary tumor where visual disturbance began nineteen years before the operation, in one eye, and four years before, in the other eye.

Clifford Walker, in a review of 271 cases showing hypophysial involvement, found 183 showing tumor manifestations, and 148 field disturbances. Of the field disturbances, 47 cases showed bilateral hemianopsia, 22 cases homonymous hemianopsia, and the remainder were blind in one eye. In other words, the bitemporal defects occur only about twice as often as the homonymous.

Valuable as the ophthalmological examination is in making a diagnosis, it is also of great aid in determining the progress of the lesion, and whether or not optic atrophy has occurred; for if it has, and is of any length of time in standing, vision will not be improved by operation.

In the roentgen examination of the sella, plates of clear detail and definition are essential—lateral stereoscopic plates of the skull at a distance preferably of 36 in. according to Hickey's experiments, making the shift from above downward toward the feet, rather than from the glabella toward the occiput, and centering over a point obtained by drawing an imaginary line from the glabella to the external auditory meatus. At a point 1¼ in. anterior to the meatus on this line, a perpendicular line ¾ in. high is erected, and through the point established at the end of the perpendicular the principal ray is passed so that it will emerge at the corresponding point on the opposite side. The floor of the sella must be sharply defined; and the anterior and posterior clinoid processes superimposed upon their opposites.

While changes in the contour of the sella commonly exist in pituitary tumor, and when found are of great help in making a diagnosis, it is however well known that enlargement of the sella with even destruction of certain or all of its parts may result from other intracranial disorders, or from tumors situated in other portions of the brain. Heuer and Dandy, in a series of 100 cases of brain tumor, report that the roentgenograms of 21 of these patients, none of whom had hypophysial or super-sella tumors, showed any destruction of the sella turcica, or atrophy of its posterior clinoid processes. Also a pituitary tumor of some size may be present, showing rather characteristic ocular phenomena, without changing the roentgen appearance of the sella.

The roentgen findings, then, of pituitary tumors may be divided into four groups: (1) No enlargement of the sella, nor erosion of the base or clinoid processes, i.e., patients without roentgen findings, (2) enlargement of the sella without erosion or destruction of the sella, (3) enlargement of the sella with thinning of the base and floor, and erosion of the clinoid processes, (4) complete destruction of the sella. To these might also be added the roentgen evidence of changes in the skull, due to general increased intracranial pressure, as enlargement of the skull, separation of the cranial sutures and vascular changes in the skull due to tumor.

Unfortunately, however, the exceedingly wide variation in the size and character of the sella noted in normal individuals who show no evidence of pituitary disturbances, permits of no absolute definite rule as to when we are dealing with early changes and variations in the contour of the sella. Since it is so essential that an early diagnosis of pituitary tumor be made, the roentgenologist must be absolutely familiar with the wide variations met in normal individuals. With this knowledge and with good technique he will be able to visualize early changes. It is important that he should note to what extent, if any, the sphenoidal sinus has been encroached upon by a tumor of the hypophysis.

The pituitary tumors most often found are adenoma, frequently with cystic developments. To quote Frazier: "About 75 per cent of pituitary tumors are adenomata.

Comparatively few are malignant and practically never metastasize to the other organs. This means that if we can prevent a recurrence of local or general intracranial pressure the life of the patient may be prolonged."

A review of the available literature shows that about 10 per cent of the adenomata of the pituitary gland develop cysts which are quite frequently very rapid in their growth. Mere evacuation by puncture gives only temporary benefit, and these cysts soon fill up again unless the operator removes a portion of the cyst wall. This is more easily accomplished by the fronto-orbital route. The prognosis is most grave in cases of sarcoma, and most favorable in cases of cysts. Walker concludes that the cases showing homonymous defects, when operated on, are not quite as successful as the bitemporal hemianopsias.

The two methods of operation most often used are Cushing's transphenoidal or submucous septal approach, and Frazier's fronto-orbital method. The mortality of each method is about the same. Frazier concludes that the cranial method is safer, for by not having to depend upon artificial illumination, one can get a better view of the tumor growth. By the endonasal or transphenoidal route, meningitis must always be reckoned with, and as a matter of fact has caused the majority of deaths following the operation, due to infection from the sphenoidal sinus. Adson of the Mayo Clinic probably favors the intradural approach, after an osteoplastic flap has been turned from the right frontoparietal region, the dura being opened widely to permit the exposure of the frontal lobe. It is well to state that it is not possible to determine accurately the extent of the lesion before operation, either by roentgen ray examination, or the ocular findings.

Dandy and Heuer, in a review of a series of 70 cases of brain tumor, state that 10 per cent of these patients were blind on admission. They believe that surgical measures, as soon as choked disc is diagnosed, should be considered, and that by operating at this time, blindness would, to a large extent, be prevented. One of the most important features of the operative technique is the control of hemorrhage. The average mortality is about 30 per cent, though Cushing and Frazier report 8 to 10 per cent in their own practice.

In a recent article, "The Effects of Radium Emanations Upon Brain Tumors," Dr. Frazier has opened up a most interesting field of investigation. Because brain tumors are often inaccessible and very difficult to localize, and because as a rule they are slow in growing, Frazier began treating them with radium, in 1914, under Dr. Henry Pancoast's direction. He quotes in his paper 3 cases in particular in which there appears to be undoubted proof that the growth of the tumors has been arrested or probably destroyed. One of these cases, that of pituitary struma, was given *x*-ray and radium treatment, the radium being directly embedded in the pituitary body through the posterior nares. This case had a return of headache and visual disturbances nineteen months after a sella decompression was performed. But after the patient had been treated as indicated above, there was a relief of the visual disturbances and headaches, and a re-establishment of menstruation.

Blumberg has recently reported 1 case of hypophyseal tumor in which disturbances of vision and beginning atrophy of the optic nerve were present in one eye, and the other eye was totally blind. In this case the trouble was brought to a permanent standstill by several series of irradiations with mesothorium.

In a short article in the A.M.A., "The Normal Sella," Dr. C. D. Enfield has well brought to our attention the wide variations in the appearance, size and contour of the normal sella, and affirmed very positively that no roentgen-ray diagnosis of pituitary tumor or disturbance should be made unless there is marked erosion or positive evidence of bony changes in the sella.

The excellent work of Dandy and his followers on ventriculography, while of most practical value in diagnosing early internal hydrocephalus, may also be of great aid in diagnosing selected cases of suspected tumor of the hypophysis, or in locating and demonstrating the presence

of the tumor in other portions of the brain, with its consequent pressure upon the pituitary gland and adjacent structures.

The recent work of Osborne, Sutherland, and Scholl, "Roentgenography of Urinary Tract during Excretion of Sodium Iodid," while primarily intended for examination of the urinary tract, offers a wide field for further investigation and possibilities along this or similar lines in the roentgen-ray diagnosis of tumors of the pituitary gland with the use of sodium iodid solution, or some other vehicle, which might aid in outlining the shadow of the tumor and other brain structures. Obviously, however, no conclusions as to the practical value of observations or work along this line can be drawn at this time.

The following recent case reports of pituitary tumors are fairly typical of the condition:

Case I. Male, aged twenty-six. Referred by Dr. M. L. Faville, a nose and throat specialist, October 15, 1920. Past history of no special significance, other than the fact that the patient has always been a little heavy for his size and has had scant beard. On September 15, 1920, he began to suffer with pain on the left side of the face. Two teeth were extracted, but this did not relieve the pain, which was dull and continuous, and much worse at night. About the middle of October, he began to notice some blurring of the left eye, which was followed in a week by a similar blurring in the right eye. There was a noticeable absence of bitemporal headaches, no change in libido sexualis, and no polyuria.

Subjective findings showed: (1) Early primary optic atrophy, (2) bitemporal hemianopsia, (3) deformity of the sella, (4) patient slightly obese.

Objective findings reported by the oculist were: "Fundus O. D. disc of normal size and shape. The temporal margin particularly is very pale, but there is a corresponding pallor of the nasal portion." *X*-ray examination on November 4, 1920, showed marked evidences of increased intracranial pressure, as shown by changes in the sella turcica. The anterior clinoid processes were definitely destroyed, the floor of the sella practically invisible, there being a definite round shadow about the size of a walnut in the region of the sella. The sphenoidal sinus was considerably decreased as a result of encroachment by the hypophysial growth. A roentgen diagnosis of pituitary tumor was made, and Dr. Faville concurring in this from his ocular findings, decided to send this patient to Dr. Harvey Cushing.

In his report to Dr. Faville, Dr. Cushing stated: "This is an extraordinary case in view of the huge sella and the complete abscence of symptoms until very recently. It is quite possible that I should have surmised a big struma containing hemorrhagic cyst. Undoubtedly it was this cyst formation from hemorrhage which led to the recent onset of symptoms."

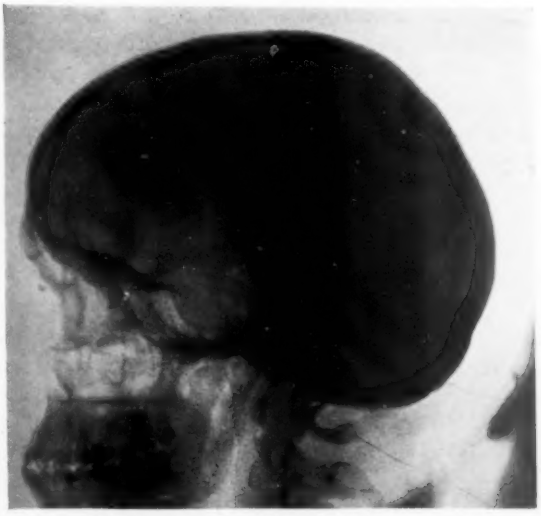

Fig. 1. Case I. Sella completely destroyed. Distinct large round shadow visible. Sphenoidal sinus encroached upon. Operative findings, hemorrhagic cystic adenoma of pituitary.

On November 13, 1920, Dr. Cushing operated, using the transphenoidal route finding the pituitary body about the size of a golf ball, with no bone whatsoever left in the floor of the sella. An incision made in the midline of the tumor showed soft yellowish gland protruding. Suddenly about 10 c.c. of dark, blackish blood gushed out, evidently a hemorrhagic cyst.

It is of interest to note further that eight months after Dr. Cushing's operation, this patient developed what was thought to be an acute intestinal obstruction. He was operated upon in Asheville, N. C., and found

to have an acute pancreatitis. He fully recovered from this operation and at the present time (September, 1923) his vision is good and he is attending to his daily work. It is an interesting speculation to what extent, if any, the disturbance of his pancreas followed the operation upon his pituitary gland.

CASE II. Male, aged fifty-two. Referred by Dr. H. B. Stone, a nose and throat specialist. Gives history of visual disturbances for the past four years, not relieved by glasses. Onset of visual symptoms gradual. Headaches, bitemporal in character, worse at night, though for the past several months have been better. Began putting on fat six years ago. Some tingling in extremities.

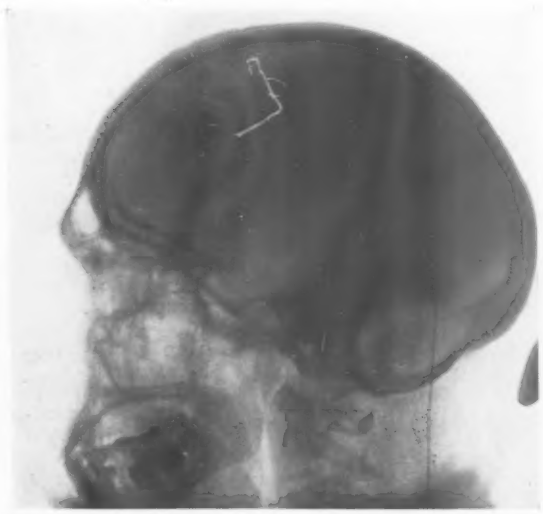

FIG. 2. Case II. Floor of sella extremely thin. Dorsum sella destroyed. Operative findings, cystic adenoma of pituitary.

First seen on August 14, 1920, at which time the sella was reported as being very deep and large, the floor and the clinoid processes not easily made out. From the roentgen findings, a tumor of the hypophysis was suggested at this time.

The patient was told to return for further examination, but did not do this until March, 1921, at which time the dorsum sella was completely destroyed. The floor of the sella was extremely thin and some encroachment on the sphenoidal sinus was noted. A roentgen diagnosis of hypophysial tumor was made.

Dr. Stone reported the following ocular findings: "Bitemporal hemianopsia. Central vision 20/30 20/50. Slight pallor of both nerve heads. Both well outlined. No choking. Terminal vessels tortuous."

Patient was referred to Dr. George Heuer of Baltimore, who operated early in April, 1921, exposing the chiasmal region by an intracranial approach. His report follows: "We immediately exposed a very large hypophysial cyst which had extended upward and directly compressed both the optic chiasm and the mesial surfaces of both optic nerves. We evacuated the cyst, which contained a bloody grumous material such as we usually find in degenerated adenomata of the hypophysis. We removed a large part of the cyst wall. Since operation the patient has done well and states that his headaches have disappeared and his vision is improved."

FIG. 3. Case III. Acromegaly. Extremely large sella. No destruction or thinning of floor. Large frontal sinus and inferior maxilla.

CASE III. Male, aged thirty-six. Illustrates the typical roentgen picture found in the secretory disturbances of the sella in the acromegaly type. Extremely large deep sella, with no destruction or thinning of the floor. Large frontal sinus, and large protruding inferior maxilla.

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IMPORTANCE OF THE ROENTGEN EXAMINATION IN THE DETERMINATION OF THE PROPER METHOD OF TREATMENT OF PULMONARY ABSCESS*

BY W. H. STEWART, M.D.

NEW YORK CITY

THE author ventures to state that the clearest and best method of ascertaining the size and location as well as the extent of involvement of the lung in all cases of pulmonary abscess, is by the roentgen examination. One can, from these findings, combined with the bronchoscopic and clinical investigations, determine the proper theraputic course to pursue.

The three recognized methods of treatment of abscess of the lung, whether single or multiple, are:

1. Expectant
2. Bronchoscopic
3. Surgical

While there is no question that a certain percentage of cases of pulmonary abscess recover spontaneously, the author is firmly convinced that one should not wait for the possibility of such an event.

Bronchoscopic treatment should be commenced just as soon as the lesion is discovered. The establishment of free drainage is an immediate indication, even though the patient have acute general manifestations; in many acute cases the simple procedure of clearing out the bronchi by suction and the opening up of the swollen and edematous branch bronchus leading to the abscess is sufficient to start resolution. More difficult cases require injection of solution of silver salts such as colline or silver nitrate. Should the process be resistant to the ordinary bronchoscopic methods, direct injections into the abscess of subcarbonate of bismuth held in suspension in sterile sweet oil can be resorted to.

It is important to check up the bronchoscopic evidence of improvement or otherwise by frequent roentgenographic examinations. No case of lung abscess is considered entirely cured until every roentgenographic sign of the lesion has disappeared. I have frequently observed that many patients, although symptom-free and gaining in weight, still show *x*-ray evidence of the process and are in danger of a "flare up."

Except in cases where hemorrhage is a complication—when instrumentation is contraindicated—pulmonary suppurations consisting of small or medium-sized abscesses located in the lower portion of the upper lobe or in the middle or lower lobes, with a moderate amount of infiltration surrounding the cavitation, seem to respond best to bronchoscopic treatment. The percentage of success in this method is largely controlled by the skill of the operator; some men are able to drain an abscess even when it is located well up in the apex.

Multiple lung abscesses or bronchiectatic cavities do not respond well to bronchoscopic treatment, and cases of pulmonary abscess complicated by a general or a sacculated empyema are entirely out of the field of the bronchoscopist.

Surgical attention is indicated in most cases of lung abscess in which there is a large amount of induration with a small amount of softening, especially if the lesion be located in the upper lobes.

Very often in cases of sacculated empyema secondary to a pulmonary abscess —and most of them are secondary—the visceral pleura has been partially or totally destroyed; this means that the case is one of pleuropulmonary abscess which can be relieved only by surgical measures. Chronic pulmonary abscesses with well-formed pyogenic membranes and rigid walls also require surgical attention.

In border-line cases the question of when bronchoscopic treatment ends and when surgery begins is a debatable one. As a rule, surgery should be resorted to if the lesion shows no improvement while under the care of the bronchoscopist for a period of six months. One case in my series received bronchoscopic treatment weekly for almost a year, with final recovery.

* Read at the Midwinter Meeting of the Eastern Section of THE AMERICAN ROENTGEN RAY SOCIETY, Atlantic City, N. J., Jan. 25–27, 1923.

It is not within the scope of this paper to deal with the different surgical requirements. It is necessary, however, for the roentgenologist to give the surgeon all the knowledge possible as to the exact location of the abscess or abscesses of the lung. Localizations by means of the *x*-ray, in positions other than the one in which the patient is to be placed on the operating table are not altogether satisfactory.

Regardless of the position in which the patient is placed, the localization must be made during a certain recorded phase of respiration, as the excursion of a pulmonary lesion with the lung during respiration is considerable. One must also be sure that the central ray is directly in the center of the shadow of the abscess, otherwise the localization may be deceiving. In addition, the relation between the abscess and certain easily recognized bony landmarks must be correctly stated. Skin marks are unsatisfactory, as the surgical skin flaps in thoracic work are considerable and the markings are either out of sight or not in correct position at the time they are needed.

The ideal method of localizing a lung abscess is by fluoroscopy in two planes made directly on the operating table, as advocated by Dr. Willis F. Manges of Philadelphia, who employs this technique especially in the localization of foreign bodies in the esophagus and bronchi.

A RELATIVELY LARGE FOREIGN BODY IN THE ORBIT

BY PERCY BROWN, M.D.

PITTSBURGH, PENNSYLVANIA

THE writer is indebted to Dr. H. H. Ainsworth of Madison, Wisconsin, for the opportunity of reporting the following interesting case:

FIG. 1.

FIG. 2.

A female child, aged two, at play, stumbled over a door-threshold while holding a piece of broken glass. Losing her balance, she fell, driving a sharp corner of the glass through the skin and subcutaneous tissue just above and external to the outer canthus of the right eye. A punctured wound of moderate severity was produced, at the orifice of which no evidence of retained foreign body was pre-

sented; neither, on account of the unknown conformation of the large fragment held by the child, could it be determined with exactitude as to whether or not a smaller fragment had been broken off. The case was treated expectantly for three weeks, and at the end of that time was referred to Doctor Ainsworth, as the local symptoms had become augmented by septic infection.

Doctor Ainsworth referred the child for examination to the Section on Roentgenology of the Jackson Clinic. The eye in question presented in moderate degree the local manifestations of infection, with much hemorrhagic injection and lachrymal hyperactivity. Photophobia was much less marked.

After some difficulty, the roentgenographic results as shown in Figures 1 and 2 were obtained. Stereoscopy seemed to be quite out of the question on account of the tender age of the child. The position of the fragment was judged to be in large measure beneath the roof of the orbit but above the globe, and so it proved at operation, with the added disclosure that there were two fragments, one larger by far than the other, as illustrated in Figure 3. This illustration also shows the dimensions of the combined fragments, believed to be extraordinary in that no intimation of these dimensions could be obtained from the appearance of the wound at the time of injury. Moreover, this complete disappearance occurred with no injury to the delicate neighboring structures, save for a very slight wounding of the superior rectus and superior oblique muscles. The patient has made an uninterrupted recovery with no functional loss.

FIG. 3.

FIBRINOUS BRONCHITIS*

BY F. HASE RODENBAUGH, M.D.

SAN FRANCISCO, CALIFORNIA

THE rarity of this lesion, considering the large number of chest examinations and pulmonary infections, and the paucity of literature containing roentgen findings constitute the basis for the report of this rather interesting case.

The diagnosis of fibrinous bronchitis is made from finding long branching bronchial casts in sputum of cases that do not have tuberculosis, diphtheria, pneumonia or some other primary bronchial disease.

In the literature there are less than 100 cases reported, and in but few of these cases are roentgen findings given. Two typical roentgenograms are those of cases described by Walker.

CASE I. *Roentgen Findings.* Diffuse peribronchial thickening throughout both lungs. Right apex showed slight mottling and left hilus slightly increased in density.

CASE II. *Roentgen Findings.* Entire right chest less radiant than left, with diffuse peribronchial thickening which is more marked on right side. Dense glands at hilus.

CLINICAL HISTORY

A brief history of the present case is quite typical with the majority of case reports:

Case III. Female, aged forty-five years. Occupation, secretary.

Past History. Unimportant; no previous pulmonary, thyroid or cardiac disturbances.

Present Illness. Onset acute with slight rise in temperature (102°F.), severe pulmonary disturbance, moderate leucocytosis with expectoration of bronchial casts.

Convalescence. Uneventful. Four months after onset of illness, patient is clinically well; an occasional small fibrin plug is expectorated.

* Paper submitted leading to membership in THE AMERICAN ROENTGEN RAY SOCIETY, 1922.

Roentgen findings during illness and following convalescence from present attack. 1. At onset: Marked increased density about hilus. Increase in bronchial tree markings in both lung fields. Diminished aeration over right lung field.

2. Six weeks: Marked increased density in left hilus over last examination. Diffuse increase in bronchial tree markings extending to lung periphery in left upper lobe.

3. Eight weeks: Left hilus shadow increased in density, less marked than at last examination. Lung fields clearer, but bronchial tree markings in both upper lobes still more marked than normal and extending to periphery.

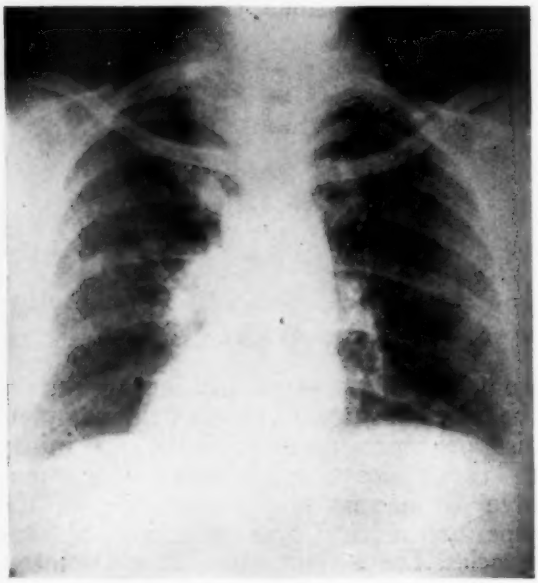

FIG. 1. At onset, Dec. 14, 1921.

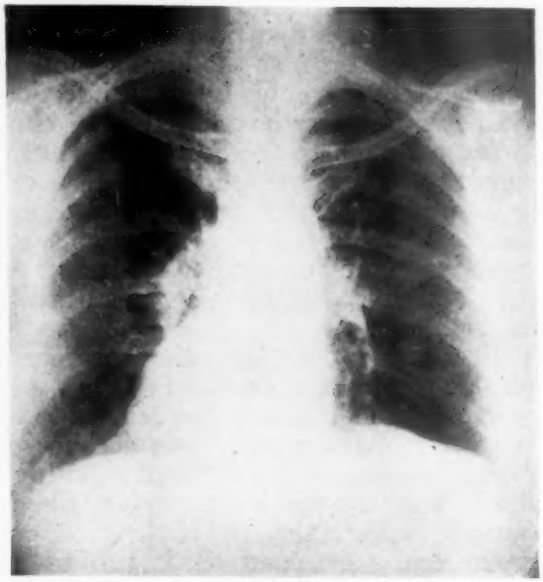

FIG. 2. Six weeks, Jan. 27, 1922.

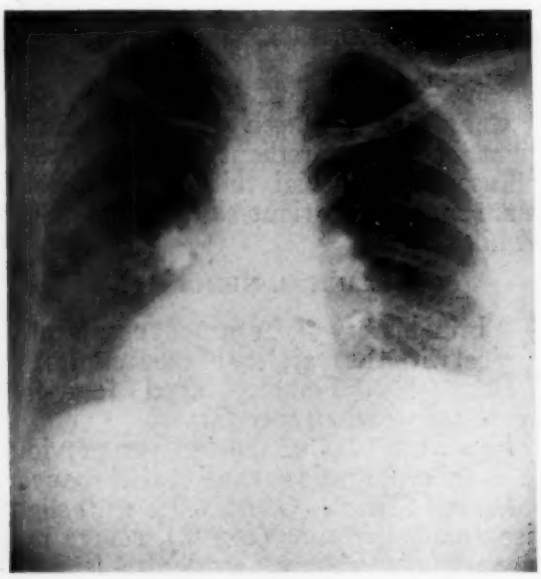

FIG. 3. Eight weeks, Jan. 14, 1922.

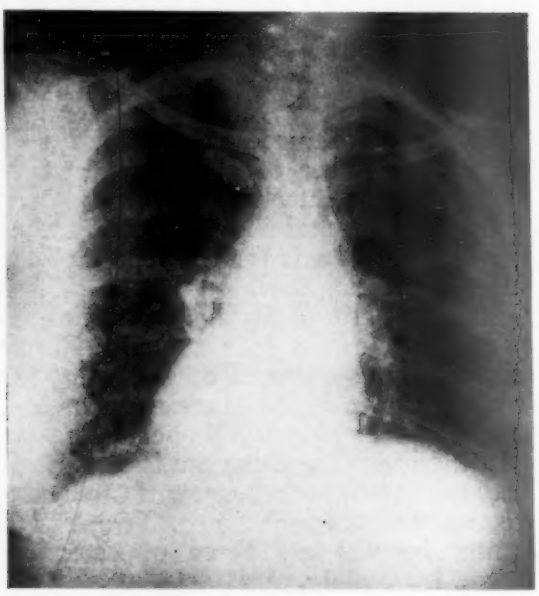

FIG. 4. Four months, Mar. 27, 1922.

4. Four months: Left hilus still showed increased density. Bronchial tree markings still present, particularly over left upper lobe, markedly decreased since last examination.

Differential Diagnosis from Roentgen Findings. The roentgen findings in this case are of considerable interest, as the pathology so closely resembles, in the distribution and character of the lung and hilus densities, certain types of pulmonary neoplasms.

An extensive review of the literature is given by Walker in *The American Journal of the Medical Sciences* for June, 1920, reviewing all cases in the literature to date. A few additional cases have been reported since; however, no additional information as to etiology or pathology has been given.

BOOK REVIEWS

DIGESTIVE DISTURBANCES IN INFANTS AND CHILDREN. By Charles Gilmore Kerley, M.D., and Leon Theodore LeWald, M.D. Contains 84 pages and 49 text illustrations in addition to 54 full-page plates; includes a note on The Surgery of Infants, by William A. Downes, M.D. Price $12. Paul B. Hoeber, Inc., New York, 1923.

The combined experience of a pathologist, a roentgenologist and a pediatrician has produced a volume of unique value for the increase of the understanding of digestive disturbances in children, and consequently for the recognition of the demand for surgical procedures necessary before the small patients have lost so much ground that they become bad risks. The special technique of examining these patients is described, while the interpretation of the findings is facilitated by the generous use of illustrations made from roentgenograms from the authors' own service. The illustrations are clearly labeled, and it is of special interest that "the diagnosis has been verified in nearly every instance by prolonged clinical observation or operation."

The differentiation between pylorospasm and congenital hypertrophic pyloric stenosis is a matter of profound importance. As for the choice of treatment of the former condition, "attention is called to the fact that roentgen examination demonstrates that the Fredet-Rammstedt operation is more desirable from a physiological standpoint, inasmuch as the stomach empties at about a normal rate after the operation; while after a gastroenterostomy it usually empties at a much too rapid rate."

Roentgen examination has also revealed that the frequently severe manifestations of syphilis in the child are often reflected in lesions of the gastrointestinal tract. A recognition of ptosis and of redundant sigmoid in the child puts the physician in a position to save trouble for the patient in later life. The influence of posture on digestion is demonstrated. Among other subjects of interest are hernia of the diaphragm, volvulus, abdominal tumors, tuberculous peritonitis and foreign bodies in the alimentary tract, in regard to which last-named subject the authors have drawn upon Chevalier Jackson's celebrated work.

The book is one which will inevitably appeal to the roentgenologist, upon whom will fall more and more of this sort of work, as its possibilities become better appreciated by the general practitioner and the pediatrist. Uniform with the other volumes in the series of "Annals of Roentgenology," the descriptive text with the illustrations appears in English, French and Spanish. The dedication is a graceful recognition of the work of Dr. Eugene W. Caldwell, "who sacrificed his life in the advancement of the science of Roentgenology." The presswork is in keeping with Mr. Hoeber's high standard.

THE AMERICAN JOURNAL OF ROENTGENOLOGY AND RADIUM THERAPY

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Information of interest to all readers and lists of officers of The American Roentgen Ray Society and The American Radium Society will be found on the two pages preceding Table of Contents.

ANNOUNCEMENT OF PLANS FOR THE FUTURE OF THE JOURNAL

In accordance with a decision reached at the Twenty-fourth Annual Meeting of The American Roentgen Ray Society held in Chicago, September 18–21, 1923, The American Journal of Roentgenology and Radium Therapy, with the beginning of the eleventh volume, January, 1924, enters upon a new era in its development. The expansion of the field of roentgenology and radium therapy calls for a larger journal, and beginning with January, 1924, there will be two volumes annually instead of one, and the journal will contain nearly double the amount of material it has had in the past.

The editorship will be in the hands of Dr. Arthur C. Christie, of Washington, D. C., whose object it will be to maintain the high standard of the Journal as in the past, and to enlarge and improve it as much as possible. Particular attention will be given to the abstract department with a view to publishing abstracts of everything worth while in the field of roentgenology and radium therapy. It is hoped, also, that the editorial department will be able to keep the readers of the Journal abreast of the progress in our specialty by reflecting every advance in its development.

Original articles will be published as promptly as possible after their receipt. In choosing articles for publication the needs of the specialist in roentgenology and radium therapy will be considered first, but due to the fact that roentgenology is rapidly taking its place in the daily work of the physician, surgeon and dentist, articles of general interest will also be included.

The Journal is to reflect at all times the present status of radiology in every phase, and whenever possible, to point the way for advance. It will be the effort of the new editor to maintain the traditions of the able editors of the past and to retain for the Journal the high position it has held.

The cooperation of our readers and of all who are interested in the advancement of medical science is earnestly solicited. Contributions, suggestions and criticisms will be welcomed by the editor.

SOUTHERN MEDICAL MEETING

The Radiological Section of the Southern Medical Association will meet in Washington, D. C. on Tuesday and Wednesday afternoons, Nov. 13 and 14, 1923.

On Wednesday evening a joint meeting of the Radiological Section and the Surgical Section of the Southern Medical Association is to be held, at which time there will be a banquet followed by papers on carcinoma of the breast. The presentation for the Radiological Section will be by Dr. George E. Pfahler of Philadelphia. The presentation for the Surgical Section will be by Dr. W. E. Sistrunk of the Mayo Clinic.

All members of The American Roentgen Ray Society and readers of the Journal are invited. We expect to have a well attended and very profitable meeting.

D. Y. Keith, Louisville, Ky., Chairman
W. R. Bethea, Memphis, Tenn., Sec'y.

TRANSLATIONS & ABSTRACTS

TAUSSIG, L. R. The radium treatment of carcinoma of the mouth. *Med. Clin. N. Am.*, 1922, vi, 383.

A large percentage of the cases referred for radium treatment at the present time are the hopeless ones which have been treated unsuccessfully by surgery or in which the seeking of expert advice has been deferred until the possibility of cure has passed. In spite of this, the number of satisfactory results has been encouraging, and soon it will be possible to recognize the class of cases for radiotherapy given alone or in combination with surgery.

The author reports three cases to illustrate the types of mouth malignancy suitable for radium treatment.

One case was that of a man forty years of age who first noticed an ulcer on the right side of his tongue about four months prior to the initial examination. The lesion was a fissure-like ulceration in a hard, nodular mass extending from just in front of the anterior pillar to within about 4 cm. of the tip of the tongue. The palpable induration projected well over the midline. Lues was ruled out by the Wassermann test. The lesion was too extensive for surgery or the actual cautery. The treatment of choice in this case was unscreened tubes of radium emanation.

The tubes were inserted in the malignant tissue rather than in the normal tissue surrounding the malignant area. The true reaction, which consists of a burning pain in the tongue and swelling, usually begins about one week later. The period and intensity of the reaction is variable. If metastatic glands develop it is advisable to remove them surgically if possible. If the condition is not operable, bare tubes of emanation should be inserted.

In the second case the author found a tumor on the inner surface of the left cheek of an upholstery worker about one year ago. The lesion was nodular, hard, about 6 cm. in diameter, and about 1½ cm. high. The glands were not palpable. Five bare tubes, totaling 9.5 mc., were inserted into the mass. On account of the suspicious appearance of the tongue, mixed treatment was given for a time under the impression that the carcinoma might have developed on a luetic base. Within a month the reaction subsided and the mass had entirely receded. Two months after treatment a hemorrhage occurred. Five months later an area of increasing thickening was noticed. Additional treatment of four bare tubes was then given. Five months ago a hard nodule developed at the tip of the tongue. Two bare tubes totaling 1 mc. were inserted into the mass. The tongue is still tender but there is no evidence of recurrence at the present time. The author feels that this case has responded well to radiotherapy.

The last case was a nodular, ulcerative, hard lesion of the posterior edge of the soft palate, involving the left side of the uvula. A course of antiluetic therapy given in spite of a negative blood Wassermann had no effect upon the growth. Four bare tubes were then inserted into the tumor. One month later one bare tube was inserted in a suspicious area on the left side of the uvula. Only one week has elapsed since the last treatment, but the entire area feels soft. The cervical region was given a course of *x*-ray treatment soon after the first bare-tube treatment.

ANDRESEN, ALBERT F. R. Linitis plastica. *Am. J. M. Sc.*, June, 1923, clxv, 799.

The author briefly summarizes the literature of the disease, referring especially to the exhaustive study made by H. M. Lyle in 1911, when he described 131 cases gathered from the literature and added 1 case of his own. Since that time not more than a dozen cases have been reported. [Undoubtedly many cases are now being seen without being reported.]—Ed.

A summary of etiological symptoms and diagnosis is included, including barium meal findings, which are referred to as including the small-sized stomach with marked hypermotility, the barium mixture passing rapidly through the upper abdomen and filling the intestinal coils. The stomach is tube-like, its walls rigid, and there is no evidence of peristaltic waves.

Two cases are reported in full, including one with an hourglass constriction occurring in the course of linitis plastica.

Roentgenograms, photographs and microscopic sections are appended, together with a brief bibliography.

BARCLAY, A. E. The organization and equipment of an *x*-ray department. *J. Röntg. Soc.*, April, 1923, xix, 55.

This is a very valuable detailed statement of the organization and equipment of a new *x*-ray department for a seven to eight hundred bed general hospital with an extensive outpatient practice. The author, however, has added a description of equipment for smaller hospitals, one of thirty and one of sixty to eighty beds. He emphasizes three very important points, namely:

1. That no elaboration of equipment can

make up for the absence of the first essential—a competent radiologist.

2. Without the provision of adequate facilities the medical officer cannot serve his purpose.

3. That every department must be laid out and equipped with an eye to the work it will be called upon to deal with.

The housing, the requirements, the equipment and the staffing of the department are all discussed in detail, and anyone in need of just the help this article can give will be well repaid by a study of this well-illustrated dissertation.

HALSTEAD, A. E., and CHRISTOPHER, F. Calcification and ossification of the meninges. *Arch. Surg.*, May, 1923, vi, No. 3, p. 847.

The authors give an elaborate review of calcification and ossification of the meninges, beginning with the first reported instance in man by Antonius Cattus in 1557. The literature is brought down to date. The authors mention that there has been to date no roentgenographic study of calcifications of the meninges. By means of stereoscopic roentgenograms of the skull it is possible to demonstrate calcified plaques in the falx and perhaps even in the parietal dura. A roentgenogram of the head of the cat reveals very plainly diffuse calcification of the falx with the sharp curving inferior border. In the case reported herewith, in which operation was performed by Halstead for tumor of the brain, the roentgen ray revealed shadows which doubtless were due to calcification in the falx.

The authors deduce that ossification and calcification of the meninges are not rare. Areas of ossification may arise from: (*a*) retention of the osteogenetic function by islands of dura; (*b*) an inflammatory process. Areas of calcification may arise as: (*a*) the result of a not far distant absorption of calcium of the skull and its subsequent deposition in the meninges; (*b*) the result of an inflammatory process. In cases of suspected brain tumor, the demonstration by means of the roentgenogram of calcification of the meninges is an additional evidence of the existence of a brain tumor exerting a circumscribed pressure on the skull. The chance finding of ossification or calcification in roentgenograms of the head affords the occasion for an intensive neurologic study of the case in question.

TARNAUCEANU. Épreuve de Goetsch et radiotherapie dans les affections du corps thyroide. (Goetsch's test and radiotherapy in diseases of the thyroid). *J. de radiol. et d'électrol.*, 1922, vi. 501.

The author recognizes the importance of some test other than the improvement of symptoms in guiding the radiologist in the treatment of exophthalmic goiter, especially with reference to the time at which each treatment should be suspended. As such a guide the author employed the Goetsch test, which consists of the subcutaneous injection of 0.5 c.c. of adrenalin solution. Tarnauceanu employed 1 c.c. instead of the 0.5 c.c. originally recommended by Goetsch.

In concluding his article the author states that in the objective and functional disturbances which it provokes the Goetsch test gives information regarding hyperfunction or dysfunction of the thyroid gland. It allows the radiologist to make a selection of patients with diseases of the thyroid and to separate those amenable to radiotherapy from those who should be treated by other methods. The Goetsch test is a rational biological test which indicates to the radiologist when the treatment should be stopped. After the completion of radiotherapy the test makes it possible to keep the patient under observation as it must be periodically repeated. It will reveal even the slightest tendency to relapse so that treatment may be renewed before the symptoms become fully apparent.

CHARRIER, A., and RIOU. Malignant Fibrochondroma of the Stomach. *Bull. et mém. Soc. de chir. de Par.*, Mar. 27, 1923, xlix, 488.

The authors report such a case in a male sixty-three years of age. There was complete transformation of the fundus of the stomach into an irregular canal with considerable infiltration of the gastric walls which had lost their elasticity and their mobility, all of which findings were based upon the barium meal. At operation a fibrochondroma of the fundus was found.

Complete histological data are given in the article.

WESSON, M. B. Pyelography: Common diagnostic errors. *Calif. State J. M.*, May, 1923, xxi, 193.

For years it has been taught that the most dangerous person in medicine is the "man with a curette," but he is harmless compared to the "amateur with a cystoscope." Pyelography is ordinarily a simple maneuver. The untoward results are due to a variety of causes, chief of which are: (1) passage of a cystoscope in a very old debilitated patient, (2) ureteral spasms and complete suppression of urine due to the trauma of passing the catheters, (3) use of toxic shadowgraph fluids, and (4) overinjection.

The illustrations show well the futility of attempting to make a diagnosis by a pyelogram

alone; a careful history and a systematic urological examination practically always result in an accurate diagnosis.

The article is illustrated by some 47 roentgenograms and photographs of very great practical value.

FISHER, E. B. Experiments on the bactericidal action of the violet ray. *Calif. State J. M.*, May, 1923, xxi, 218.

These experiments seem to indicate that the benefit derived from the violet ray is not from its ability to destroy bacteria but rather its power to increase the number of leucocytes.

FABER. Gastroptosis and the shape of the thorax. *Ugesk. f. Laeger*, May 11, 1922.

Faber finds that the frequency of gastroptosis increases considerably with the degree of deformity and narrowing of the chest. The position of the stomach, as shown by the *x*-rays after a "contrast" meal, and when the patient stands up, may be such that (1) it is entirely above the umbilicus; (2) the lesser curvature is above, the greater below the umbilicus; (3) the lesser curvature is 2 cm. or less below the umbilicus; or (4) it is at least 2 cm. below the umbilicus. The author has devised what he calls the "epigastric index." A line is drawn from the umbilicus to the lower end of the sternum. At the middle point on this line a horizontal line is drawn from one costal arch to the other. The epigastric index is obtained by multiplying the length of this horizontal line by 100 and dividing by the length of the vertical line. The author finds that the average epigastric index is 59.3 for men and 45.4 for nulliparous women. A high index was usually associated with a high position of the stomach among men and nulliparous women. But in parous women there was little relation between the epigastric index and the degree of gastroptosis, which was evidently determined chiefly by childbearing. One of the author's patients was a tall, thin woman with an epigastric index of 30 and the lesser curvature of the stomach several centimeters below the umbilicus. After six years, during which her weight rose from 46 to 80 kg., the lesser curvature was 8 cm. and the greater curvature 3 cm. above the umbilicus.

CROWE, S. J., and BAYLOR, J. W. Benign and malignant growths of the nasopharynx and their treatment with radium. *Arch. Surg.*, Mar., 1923, vi, 429.

The principal object of the article is to report the authors' experiences with the use of radium as a therapeutic agent in nasopharyngeal growths; but also to emphasize the fact that the growth must be recognized early in its development in order to improve our present therapeutic results.

Results with the radium treatment of lymphosarcoma of the nasopharynx are not good, although this variety of sarcoma disappears locally after irradiation more rapidly than does any other type of tumor with which we are familiar. One possible explanation for this unsatisfactory clinical result is that the earliest symptoms of lymphosarcoma in the nasopharynx are difficulty in breathing through the nose and Eustachian tube obstruction, and that these symptoms are usually treated without recognition of the underlying cause until the growth has become diffused throughout the body. The authors believe that it would be a wise precaution to treat with radium every adult patient that has a localized hypertrophy of the lymphoid tissue limited to the nasopharynx, rather than to remove this hypertrophied tissue with a curette.

In this paper little is said about the detailed technique of irradiation. Radium as a therapeutic agent is more dangerous than the roentgen rays, and should be employed only by those who, in addition to their medical education, are thoroughly familiar with physics and higher mathematics. A large clinical experience and a careful correlation of dosage, method of application and result, in the various types of new growths, are essential for the training of a radiologist. For example, it is conceivable that a physician or surgeon, untrained in biophysics, might advise a patient with a localized lymphosarcoma in the throat to have prophylactic irradiation of the mediastinum, abdomen and the glands in the axilla and groin, but a physicist would recognize immediately that such a plan of treatment would result in profound changes in the blood and probably hasten the death of the patient.

The authors discuss polypi, nasopharyngeal fibroma, angiosarcoma (lymphosarcoma, angiosarcoma, myxosarcoma) and cancer.

None of the various types of polypoid growths that occur in the nose or nasopharynx has a rich blood supply, and excessive bleeding following the removal of a polyp always suggests that the primary cause may be a malignant growth instead of an infection.

Irradiation has but little influence on the size or growth of polypoid or myxomatous tissue. The authors have never implanted either radium or its emanations into a nasal polyp: but they have repeatedly irradiated heavily both intranasally and externally without curing the polypoid condition.

In nasopharyngeal fibroma, although the authors' experience has been limited to 4 cases, 2 of these are well and the other 2 are improving.

The treatment consisted of a combination of implantation of emanations, intranasal and external irradiation, and partial removal by operative methods.

For angiomas it is probably deleterious to the best interests of the patient to remove a piece of the growth for microscopic examination, and it is certainly not advisable to attempt the removal of the large nasal growths of this type through the nose. The fact that a piece of the growth had been removed was undoubtedly responsible for the frequent and severe hemorrhages in 4 of the authors' 5 cases that presented this symptom.

With reference to sarcomas, the authors emphasize that every growth removed from the nose and throat should be investigated, grossly and microscopically; but, on the other hand, the diagnosis of such growths should not be based on the microscopic appearance of a small fragment, without taking into consideration all of the clinical and laboratory data that are available. It is doubtful, indeed, whether the removal of a piece of a tumor for diagnosis is ever a justifiable procedure. It is possible, however, that incomplete operative removal or even the removal of a small fragment, either before or during the irradiation, is responsible for the reappearance of the growth in some distant part of the body. If the growth is a very vascular sarcoma or a true angioma, the deleterious effect of a partial removal is apparent in the increased frequency and severity of the hemorrhages. In the majority of the authors' cases of sarcoma, angioma and fibroma bleeding was not a prominent symptom until a portion of the growth had been removed. After the nasal operation, however, the growth becomes infected, and hemorrhages are severe and frequent.

PHEMISTER, D. B. The nature of cranial hyperostosis overlying endothelioma of the meninges. *Arch. Surg.*, Mar., 1923, vi, 554.

This is an extremely interesting study of the local changes in the skull overlying meningeal endothelioma. After a historical summary the author reports 2 cases with photographs, roentgenograms and microscopic sections.

The hyperostosis which develops over a considerable proportion of meningeal endotheliomas results from penetration of the dura and direct invasion of the skull by the tumor. The tumor permeates the skull, rarefies slightly the inner and outer tables and stimulates new bone formation, usually from both the internal and external surfaces. Tumor cells are found in varying numbers throughout the cancellous spaces of the hyperostosis. The new bone is not tumorous in nature, and is merely ossified stroma of the invading endothelioma. Its spongy or radiating arrangement is similar to that which is seen in the ossification occurring in other types of tumor, whether primary or secondary in bone and whether the new bone itself is of tumorous or nontumorous nature.

VINSON, PORTER P. Cardiospasm associated with esophageal diverticula. *N. York M. J.*, May 2, 1923, p. 541.

Diverticula of the middle portion of the esophagus have been observed rather often at post-mortem, but rarely have been demonstrated during life. They occur usually in the region of the left bronchus, and are due to healing processes following inflammatory lesions in the periesophageal glands. However, Le Count and Brosch have reported small diverticula of the thoracic esophagus apparently not caused by inflammatory reactions, but by lack of support of the esophageal wall. The contraction of fibrous tissue pulls a small portion of the esophageal wall outward and upward, and produces the so-called traction diverticula. The apices of such diverticula point upward, so that there is no tendency for ingested food and fluid to accumulate in them and increase their size, as is the case in pulsion diverticula.

The author reports 2 cases seen in the Mayo Clinic, in which a pouching of the left side of the middle of the esophagus was found in addition to obstruction at the cardia with the findings typical of cardiospasm.

The mechanism of the formation of these diverticula is, of course, purely speculative. They may have resulted from congenital weakness of the esophageal wall, or they may have had their origin in tiny traction diverticula. In either case they could not have attained considerable size without the spasm at the cardia causing retention in the esophagus, and adding the pulsion force necessary to increase the size of the pouch. It is interesting that neither of the patients had symptoms suggesting that the diverticulum was a factor in the production of the dysphagia. It is possible that the second patient will have food obstruction from the diverticulum at some future time, but if this occurs, food can be given through a stomach-tube which has been guided beyond the sacculation on a previously swallowed silk thread.

SIMONETTI. Contribution to the study of gastric stimulation by *x*-rays. *Gaz. d. osp.*, Jan. 14, 1923, xliv, No. 4.

The roentgen ray employed in weak doses does not produce a destructive effect such as is commonly employed in therapeutics, but, on

the contrary, exercises a stimulating effect upon cellular activity. Under the action of *x*-rays the total acidity of the gastric juice is constantly increased after ten or twelve such applications. This hyperacidity seems to consist of an increase in the free hydrochloric acid. The pepsin measured in 12 patients after the ingestion of a definite quantity of albumins was found increased in 8 cases, diminished in 3 and unchanged in 1. Clinically this increase of the different components of the gastric juice should be manifested by a return of appetite and more satisfactory digestion of the food. The improvement may come on immediately or some days after the last application.

RAND, CARL W. Osteoma of the skull. *Arch. Surg.*, Mar., 1923, vi, 573.

The author reports 2 cases of osteoma of the skull, one being associated with a large intracranial endothelioma. Numerous roentgenograms and photographs of microscopic sections illustrate this paper.

REVERCHON ET WORMS. Valeur séméiologique de la radiographie dans l'étude de la polysinusite grippale. *Presse méd.*, May 12, 1923, p. 440.

The authors were able during the last winter to study roentgenographically 12 cases of polysinusitis following grippe, both in the acute period and after cure. The series of plates made permitted the authors to follow the ebb and flow of the inflammation which showed a tendency to spontaneous cure as long as drainage was maintained. At the beginning there was a definite shadow, especially in the region of the ethmoid which masked without changing the anatomical outlines. This shadow rapidly extended to the maxillary sinus, then to the frontal sinus and often involved the sphenoid. The sinuses became clear in the inverse order from that in which they became obscured. Transparence reappeared first at the level of the maxillary and frontal sinuses and then in the ethmoidal region, which proved to be the last to return to the normal state.

The information given by roentgenography as to the evolution of a post-influenzal polysinusitis permits a better comprehension of the reasons for temporizing treatment.

DE JONG, S. I., and AUBOURG. A case of perisigmoiditis verified by roentgen ray study. *Bull. et Mém. Soc. Méd. d. hôp. de Par.* Mar. 22, 1923, No. 10, p. 423.

The authors report in detail, including roentgenograms, the complete story of a case of a plastic sigmoiditis. In this instance the plastic exudate finally was spontaneously re-absorbed without any treatment whatever.

ASHHURTS, A. P. C., BROMER, S. R., and WHITE, C. Y. Cystic disease of the bones. *Arch. Surg.*, May, 1923, Vol. vi, 661.

This is a surgical, roentgenological and pathological consideration of cystic disease of the bones based on a study of 15 cases. These cases are carefully narrated, but the article hardly lends itself to abstract.

MAXIMOW, A. A. Changes produced by roentgen rays in inflamed connective tissue. *J. Exper. M.* xxxvii, 319.

Maximow studied the reaction of inflamed tissue, the result of a foreign body, to the roentgen rays. He noted that irradiation produced a considerable depression of the usual reaction on the part of the fibroblasts. They remain idle, do not multiply at all, or start very late and often the division is abnormal. Simultaneously with these changes of the fibroblasts, an intensive edema of the connective tissue surrounding the foreign body is to be noted and in the immediate neighborhood of the latter a thick layer of net-like clotted fibrinous exudate is formed. No distinctive qualitative changes could be found in the leukocytes and polyblasts. The rate and the duration of the emigration of all the cells coming from the blood were increased, and there was always a distinct delay in the process of the common transformations usually undergone by the polyblasts on the field of inflammation. The transformation of the polyblasts into fixed resting forms seems, above all, to be delayed. In the blood-vessels swelling of the endothelial cells, with fragmentation of the nuclei, and, in the striated muscles, degeneration of the fibers can be detected. In the latter there occur partly typical coagulation necrosis, partly atrophy, accompanied by loss of striation, separation of fibrillae from one another, relative increase of sarcoplasm, and amitotic division of nuclei. These results seem not to agree with the predominating views on the action of roentgen rays on cells.

SYMONDS, C. Gonorrheal stricture of the rectum. *Proc. Roy. Soc. Med.*, 1923, xvi, 13. Sect. Surg.

This type of stricture involves the lower 8 or 10 cm. of the rectum, including the anal margin and the entire circumference of the bowel. The bowel shows bands and bridles of indurated muscle separated by pockets, from the bottom of which fistulous tracts lead into the vagina or to the surface around the anus. In advanced cases it is not possible to make a digital

examination because of the extreme narrowing which occurs.

All 7 of the cases reported by the author occurred in women. In searching the museums he was able to find 38 other specimens, many of these being labeled "syphilitic in origin." It is entirely probable that many cases of syphilis of the rectum are in reality gonorrheal in origin.

Colostomy is the principal indication with cecostomy or appendicostomy as a substitute in certain cases. It is dangerous to attempt dilatation because the use of bougies or division of the stricture is likely to produce a perforation. Excision can seldom be performed except when the disease is very early.

RHORMLEY, R. K. A case of congenital osteosclerosis. *Johns Hopkins Hosp. Bull.*, 1922, xxxiii, 444.

The author first carefully reviews the literature, noting that the condition described had not been reported as diagnosed during life in any case. Several cases were diagnosed at autopsy.

In the author's case the diagnosis was first considered as a beginning epiphyseal separation of the head of the left femur. Roentgenographic study of the pelvis showed a peculiar density of the bones, and a later study of all the bones revealed practically the same condition throughout the entire skeleton; the vertebral bodies even showed marked density at both poles; the ribs showed thickening of the cortex of the bones, especially in the distal portion of the long bones; the skull was thickened. In the neck of the femur on both sides, especially in the left side, there seemed to be a destruction of the bone just below the peiphysis. The condition was proved to be congenital by a study of the father's bones, which were exactly like those of the child. The mother's bones were shown to be roentgenologically normal.

BALDWIN, W. M. A study of the combined action of *x*-rays and of vital stains upon paramaceia. *Biol. Bull.*, 1920, T. xxxix. 59.

The author has made use of a certain number of vital colors, Nile blue, alizarin blue, trypan blue, isamin blue, dahlia and other colors. The author also employed the *x*-rays and has observed the successive action of the colors and of the *x*-rays. While the quantity of energy necessary to inhibit the activity of the non-colored paramecia varied from 60 to 80 ma. minutes under the conditions of the experiment, on the other hand, with the colored infusoria, for example, those colored with trypan blue, the same result was attained in 5 to 10 ma. minutes. There are, nevertheless, considerable variations within certain limits in the sensibility of the various cultures to the energy of the *x*-rays and also in the rapidity with which they absorb the colors. The direct application of *x*-rays upon the colors themselves did not seem to modify their action upon the infusoria.

SCHINZ, H. R. Human castration by the *x*-ray (Ein Beitrag zur Roentgen-Kastration beim Mann). *Schweiz. med. Wchnschr.*, 1922, lii, 866.

After reciting a case in which castration was performed in a man by means of the *x*-ray, the author describes the physiological effects of the dose given and makes the following suggestions regarding the determination of the dose and the clinical signs upon which the size of the dose should be based:

1. Temporary sterilization with clinical oligonecrospermia. Necessary dose, at least 34 per cent of the skin unit dose in the male; 30 per cent in the female.

2. Total permanent aspermatogenesis. Dosage, about 60 per cent of skin unit dose in the male; in the female with Wintz exovulation, 32 per cent.

3. Total castration with destruction of all the constituent elements of the testicle. Dose for male not yet determined; for the female, 34 per cent of the skin unit dose.

BIERMAN, M. I. and JONES, W. M. A Third Omentum. *Surg., Gynec. & Obst.*, May, 1923, xxxvi, 641.

The authors have chanced upon 2 cases, in each of which there was an additional omentum much like the greater omentum; but instead of being dependent from the transverse colon it was dependent from the lesser curvature of the stomach. At operaton no pathological conditions of any kind were found in the upper half of the abdomen. The additional loop of omentum, therefore, was not the result of an inflammatory condition in which there had been a separation of omentum in an attempt to localize an inflammatory process, but appeared to be a distinct developmental variation.

A semi-diagrammatic sketch is appended of one of the case reports where this third omentum extended from pylorus to cardia, being triangular in shape, and its length almost half that of the circumference of the stomach. The omentum was curled up during the roentgen examination and produced a constant defect on the lesser curvature. When found, it was still partly folded up but was straightened out without any difficulty. Such a possibility should be borne in mind by every roentgen diagnostician.